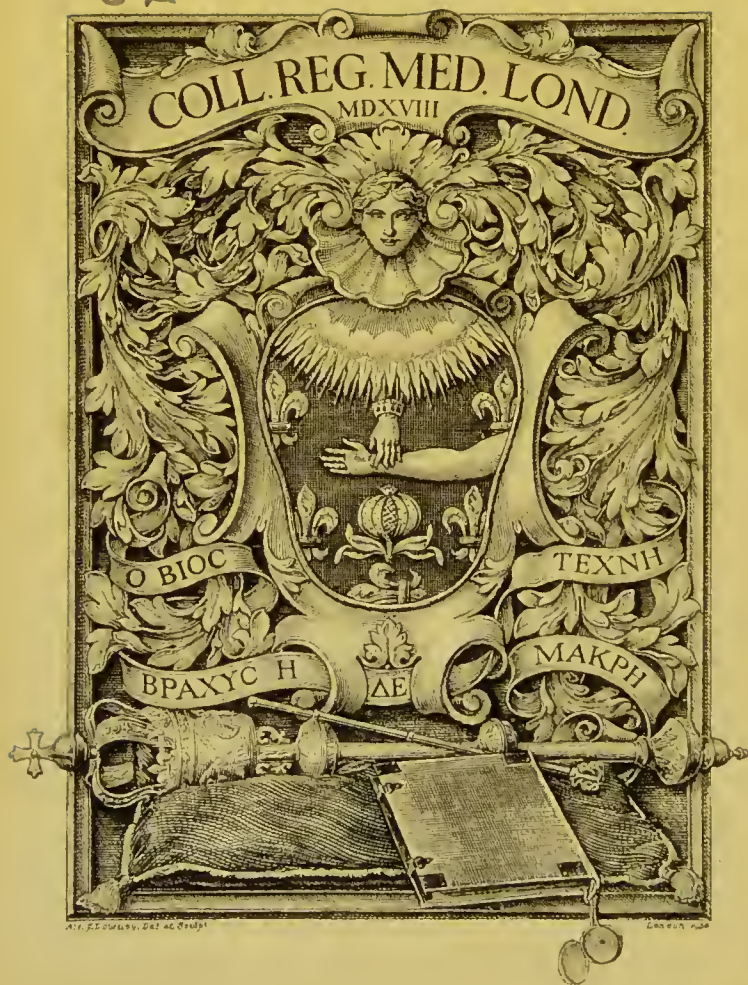



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JAUNDICE

Definition.—Jaundice is the condition due to the presence of bile-pigment in the blood, and is recognised clinically by staining of the skin, conjunctivae, mucous membranes, blood-serum, and, as a rule, of the urine, by bile-pigment.

Like albuminuria, it is a symptom and not a disease, and may be met with in a number of different conditions, ~~the common and essential factor being obstruction at some point to the passage of bile along the bile capillaries or ducts.~~

Etymology.—The word jaundice is derived from the French *jaune*, yellow. Wickham Legg¹ gives several possible derivations for icterus, such as *ἰκτίς*, the yellow-breasted marten, which probably was the equivalent in ancient Greek households of our domestic cat; *ἰκτερος*, the golden oriole, the sight of which was supposed to cure jaundice, whereas the bird died (Pliny); and from *ἰκτίvos*, a kite, from the colour of its eyes.

Introduction.—The formation of bile-pigment from haemoglobin is limited to the cells of the liver and cannot be vicariously carried out elsewhere in the body, for, as shewn by experiments on animals, this transformation does not take place when the liver is removed, or—and this comes to the same thing—when all the vessels going to it are ligatured.

Moleschott² shewed that after excision of the liver in frogs there was no formation of bile in any part of the body; and by excluding the liver of pigeons from the circulation by ligature of its vessels, Stern³ and Minkowski and Naunyn,⁴ in ducks, proved that the same was true in birds.

It has, however, been argued that since haematoidin, which is chemically identical with bilirubin, is formed in old haemorrhages from haemoglobin, bile-pigment may be similarly manufactured in other parts of the body.

Jaundice, or the presence of bile-pigment in the blood, is due to the passage of bile, manufactured by the liver, into the circulation instead of into the intestines. This miscarriage of the bile may occur either directly the bile-pigment is formed by the liver cells—*i.e.* before the bile enters the bile-ducts—or later, after it has passed into the ducts. It has been suggested by Frerichs, Liebermeister, Szubinski, Minkowski,⁵ and Pick⁶ that in certain conditions, such as toxæmia, the normal secretion of bile

¹ Legg, J. Wickham. *Bile, Jaundice, and Bilious Diseases*, 1880, p. 225.

² Moleschott. *Arch. f. physiol. Heilk.*, 1852, xi, 479.

³ Stern. *Arch. f. exper. Path. u. Pharmacol.*, 1885, xix, 39.

⁴ Minkowski und Naunyn. *Ibid.*, 1886, xxi, 1.

⁵ Minkowski. *Verhandl. d. Congr. f. inn. Med.*, Wiesbaden, 1900, xviii, 316.

⁶ Pick, A. *Wien. klin. Wchnschr.*, 1903, xvi, 493.

may be so disturbed that the bile passes direct into the lymphatics or blood-vessels of the liver instead of into the bile capillaries (diffusion or acathetic jaundice, jaundice from parapneumonia, paracholia). This hypothesis has been employed to explain jaundice in cases in which no obstruction can be found; especially in chronic haemolytic jaundice (*vide* p. 537). There are two views as to the path by which bile passes: from the bile-ducts into the circulation in obstructive jaundice; the experiments of Saunders¹ (1803), and later of Fleischl,² V. Harley,³ and Szubinski⁴ shewed that the bile enters the lymphatics of the liver, and that jaundice due to ligature of the bile-duct can be removed or prevented by ligature of the thoracic duct. On the other hand, experiments have been brought forward to prove that the bile enters the blood-vessels, and that a fistula of the thoracic duct does not influence jaundice (Mendel and Underhill,⁵ Wertheimer and Lapage,⁶ Whipple and King⁷).

Obstruction in the ducts leads to a rise in the pressure of the bile, which is normally low, and, as a result, the bile passes into the general circulation. This clearly explains the production of jaundice in cases in which there is a gross mechanical obstruction in the ducts, but it is necessary to consider further the method of causation of jaundice in cases without any manifest obstruction in the larger bile-ducts.

Pathology of Jaundice.—Jaundice was formerly divided into: (i) Hepatogenous or obstructive, due to manifest obstruction in the larger bile-ducts, and (ii) so-called non-obstructive, in which there was no gross obstruction in the course of the bile-ducts. This form included (a) jaundice thought to be due to haemolytic changes in the blood, which consisted in the liberation of haemoglobin and its transformation in the circulation into bile-pigment; this was spoken of as *haematogenous jaundice*. (b) *Jaundice from polycholia*, in which an excessive secretion of bile was followed by such free absorption of bile by the mucous membrane of the intestine and bile-passages that some of it overflowed into the general circulation. (c) *Jaundice by suppression*, in which the cells of the liver were supposed to strike work and no longer form bile. As a result an accumulation of bile-pigments, manufactured in the general circulation, was thought to occur. As in the first-mentioned form (haematogenous jaundice), this explanation was based on the assumption that bile-pigments could be formed elsewhere in the body than in the liver. (d) "Urobilin" jaundice.

(a) *Haematogenous and Haemolytic Jaundice.*—In various toxic and infective conditions which cause haemolysis slight jaundice is often seen. A good example of this "toxaemic" jaundice is provided in the experi-

¹ Saunders, W. *A Treatise on the Structure, Economy, and Diseases of the Liver*, p. 111, 3rd ed., 1803, Lond.

² Fleischl. *Arch. u. d. physiol. Anst. zu Leipz.*, 1874, ix, 24.

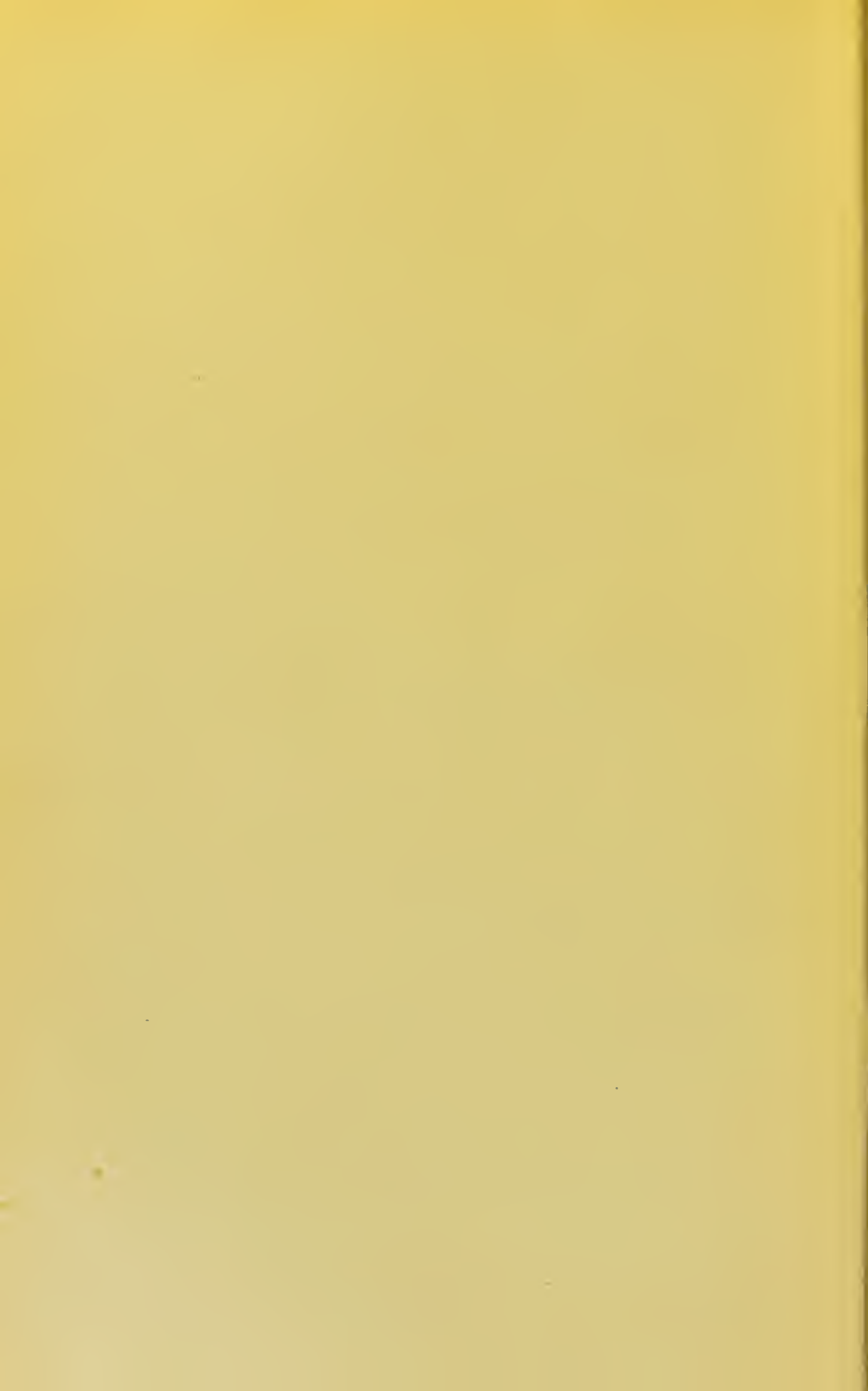
³ Harley, V. *Arch. f. Anat. u. Phys.*, 1893, S. 291.

⁴ Szubinski. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1899, xxvi, 446.

⁵ Mendel and Underhill. *Am. Journ. Physiol.*, 1905, xiv, 252.

⁶ Wertheimer et Lapage. *Arch. de physiol.*, Paris, 1898, 5. s., x, 334.

⁷ Whipple and King. *Journ. Exper. Med.*, N.Y., 1911, xiii, 115.



ments of Stadelmann¹ and Hunter² with toluylenediamine. This poison destroys the red blood-corpuscles with liberation of haemoglobin (haemolysis) and causes jaundice. After its administration there is at first a more copious flow of bile containing an increased quantity of bile-pigments (polychromia), owing to an augmented amount of free haemoglobin, the antecedent of bile-pigment, reaching the liver. After a time the bile diminishes in amount and becomes more viscid, until finally its flow is almost arrested. This slowing and diminution in the flow of bile depend on inflammation of the smaller intrahepatic bile-ducts, which become swollen and contain thick mucus as a result of the toxic action of the toluylenediamine. The jaundice, therefore, is really due to obstruction, which, being situated in the small intrahepatic ducts, is readily overlooked. This explanation accounts for the comparatively slight jaundice seen in septicaemia, pyaemia, haemoglobinuric fever, pernicious anaemia, phosphorus and other forms of poisoning, and snake-bite. Eppinger³ finds that in these circumstances the bile capillaries become obstructed by coagulated bile, and that this leads to the passage of bile into the lymphatics. The jaundice is, therefore, toxaemic, and is dependent on changes (inflammation and obstruction) in the small intrahepatic bile-ducts, produced by poisons in the general circulation. It may be appropriately spoken of as intrahepatic or haemo-hepatogenous jaundice, but not, as it formerly was, as "haematogenous" jaundice. Experiment shews that the presence of free haemoglobin in the blood, though it leads to an increased secretion of bile-pigment in the bile (polychromia), does not of itself give rise to jaundice. In practice jaundice is often seen in cases in which extensive haemolysis or destruction of red blood-corpuscles is taking place. The two phenomena are regarded by Hunter as the associated but independent results of infective or toxic factors which destroy the red blood-corpuscles and at the same time excite inflammation of the intrahepatic bile-ducts.

Paroxysmal haemoglobinuria, though usually, is not necessarily, associated with jaundice. In pernicious anaemia haemolysis ~~in the portal area~~ is a ~~very~~ ^{well} marked feature, but the jaundice is slight and may be practically absent. On careful microscopic examination of the liver in pernicious anaemia catarrhal inflammation of the small bile-ducts may be seen in some instances.⁴

On the other hand, opinion is now inclining to the view that jaundice may in certain conditions be independent of any obstruction in the biliary apparatus and truly haemolytic in origin (*vide* p. 538).

(b) *So-called Jaundice from Polycholia*.—When jaundice was found to be associated with bile in the faeces, it was supposed that there was such a profuse secretion of bile (polycholia) that an excessive amount of bile was absorbed from the mucous membrane of the intestines and bile-

¹ Stadelmann. *Der Icterus u. seine verschiedenen Formen*, Stuttgart, 1891.

² Hunter, W. *Journ. Path. and Bacteriol.*, 1896, iii, 259.

³ Eppinger. *Ergebnisse der inneren Medizin und Kinderheilkunde*, 1908, i, 107.

⁴ Compare Bret et Cade. *Lyon méd.*, 1902, xcix, 457.

passages and passed through the liver into the general circulation. Bile may be present in the faeces of jaundiced patients under various conditions; thus in obstruction of one hepatic duct icterus results, but the other hepatic duct pours bile into the duodenum. A calculus in the common duct may act like a ball-valve and allow bile to escape into the bowel at intervals; and in biliary cirrhosis bile is usually present in the faeces. In none of these examples is there any suggestion that an excessive secretion of bile exists. In toxæmic jaundice there is in the early stage a secretion of bile rich in bile-pigment (polychromia) and poor in bile acids, the pigment appearing in the excreta; obstruction in the small ducts subsequently occurs, and produces jaundice. This is the explanation of so-called jaundice from polycholia. But it should be pointed out that, strictly speaking, there is not an excessive secretion of normal bile (polycholia), but only of bile-pigment (polychromia), and that the bile-salts, far from being increased, are diminished.

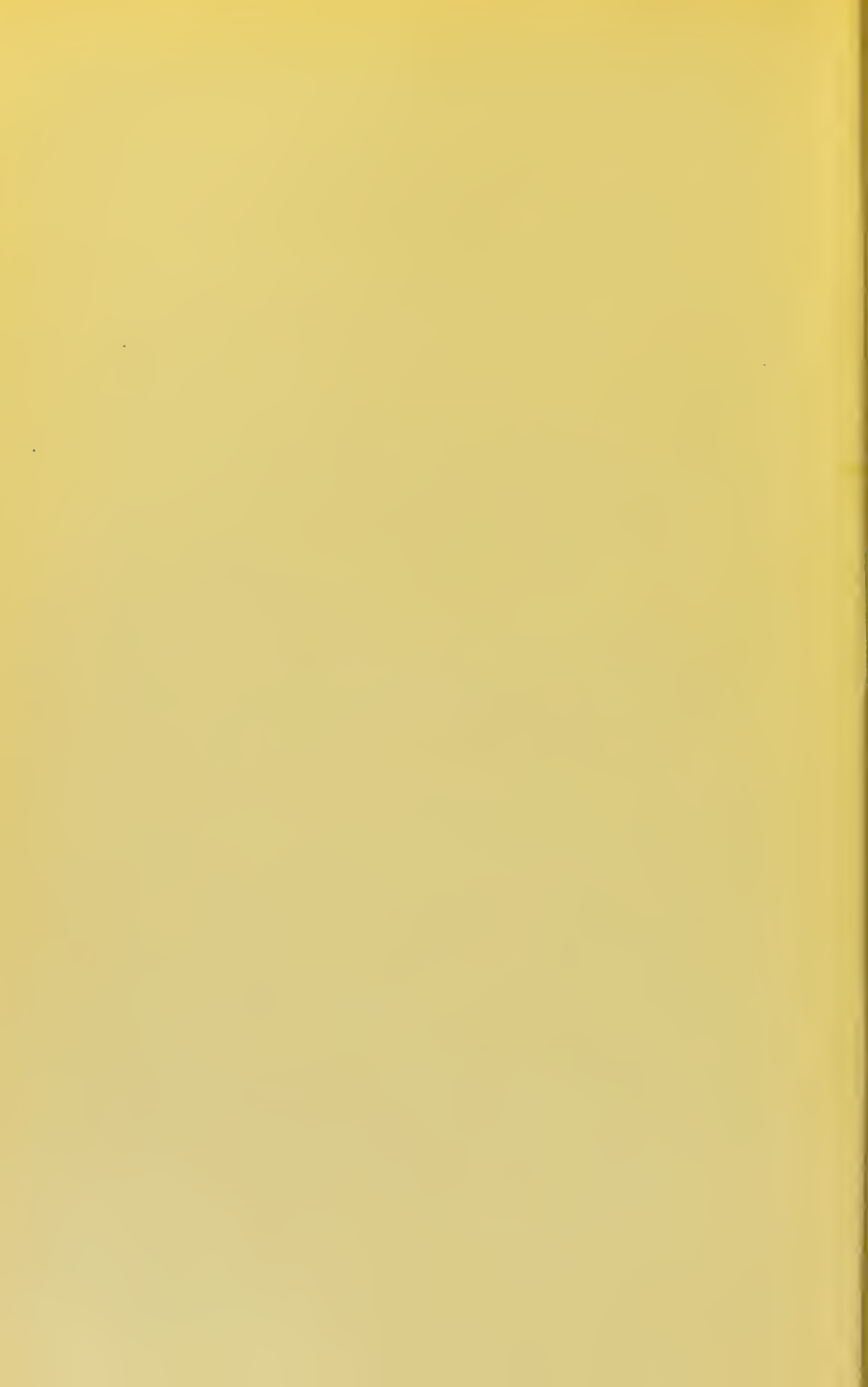
(c) *The So-called Jaundice from Suppression of the Bile-secreting Function of the Liver.*—It was formerly supposed that the liver might, from nervous or other influences, cease to secrete bile, and that an accumulation of refuse blood-pigment in the circulation resulted, which became changed, without the intervention of the liver, into bile-pigment.

There is no proof that in jaundice the liver does strike work. In acute yellow atrophy and phosphorus poisoning the jaundice is almost certainly due to obstruction in the small intrahepatic ducts from inflammation, and to the passage of bile into the lymphatics, which results as a natural consequence. In long-continued biliary obstruction the ducts contain clear mucous fluid devoid of bile, and it was formerly thought that the liver ceased to secrete bile under these conditions; but the liver cells, as shewn by the presence of bile-pigment inside them, still manufacture bile, which passes almost directly into the circulation.

(d) *"Urobilin" Jaundice.*—(*Synonyms: Haemophaeic Jaundice; Acholuric Jaundice.*)—These terms have been applied to cases in which, though the skin is yellow, there is no bile-pigment in the urine. It has been thought that staining of the skin indistinguishable from jaundice may be due to pigments other than those of bile—either urobilin or a hypothetical product of haemoglobin called haemophaein (Gubler). The reason for supposing the pigmentation of the skin to be due to urobilin was that in such cases the urine often contained an excess of urobilin. But in such cases the blood-serum, obtained from a blister or from other sources, is found to contain bile-pigment in small quantities and not urobilin¹; hence the condition is one of true jaundice, and the terms "urobilin" and "haemophaeic" jaundice are erroneous and misleading. Excessive urobilinuria may occur in cases of toxæmic jaundice in which bile-pigment is temporarily absent from the urine. To this condition the term "acholuric jaundice" has been applied (Gilbert and Herscher²). Cases formerly called urobilin jaundice are, therefore, mild cases of jaundice in which a

¹ Compare Thiele. *Trans. Path. Soc., Lond.*, 1903, liv, 62.

² Gilbert et Herscher. *Presse méd.*, Paris, 1902, 1239.



sufficient amount of bile-pigment passes into the circulation to stain the skin, but not enough to be present constantly in the urine. The excess of urobilin in the urine is probably due to the action of bacteria on bile-pigment in the intestine, though Gilbert and Herscher¹ consider that the urobilin is manufactured by the kidneys from bile-pigment present in the blood-serum. This form of jaundice is sometimes seen in portal cirrhosis and in gastritis, and may be due to a slight secondary infection of the ducts from the duodenum (Hayem²). On the other hand, it may be a mild form of toxæmic jaundice. The condition is closely allied, according to Gilbert and Herscher, to simple family cholaemia (*vide* p. 40), described by Gilbert and Lereboullet,³ and differs from it in the urine being more concentrated.

Classification.—Jaundice may be divided, therefore, into—(1) *Extra-hepatic* or “*obstructive*,” in which there is a gross obstruction, usually involving the large, extra-hepatic bile-ducts, to the flow of bile along the bile-ducts. (2) *Toxæmic, intrahepatic*, or *haemo-hepatogenous*, in which there is in most cases obstruction in the small intrahepatic bile-ducts. The obstruction is due to cholangitis or inflammation of the minute ducts, depending on the irritating effect of poisons derived from the blood circulating through the liver. A reservation as to the presence of cholangitis is necessary, for it has recently been urged that in chronic haemolytic jaundice there is no inflammation or obstruction in the bile-ducts (*vide* p. 538).

Jaundice is, therefore, a symptom, not a disease in itself. It may be the result of a purely local condition, namely, a tumour pressing on the large extra-hepatic bile-ducts; or, on the other hand, it may primarily depend on a general infective or toxæmic process.

Toxæmic, Intrahepatic, or Haemo-hepatogenous Jaundice.—This form of jaundice, in which there is no gross obstruction to the flow of bile through the larger bile-ducts, is usually obstructive and due to inflammation of the small intrahepatic bile-ducts (angiocholitis) set up by poisons reaching the liver by the blood-stream. Toxæmic jaundice is met with in numerous conditions which may, for convenience, be divided into three groups: (i) various infections; (ii) as the result of certain poisons or drugs; (iii) chronic splenomegalic haemolytic jaundice.

(i) It may occur in a number of diseases, especially hæmic infections, such as pyæmia, septicæmia, relapsing fever, hæmoglobinuric fever, and may be seen in pneumonia, typhoid fever, pernicious anaemia. In some instances, as mentioned above, jaundice may be associated with hæmolysis, for example, in paroxysmal hæmoglobinuria; the jaundice, however, is not a necessary result of hæmolysis, but a concomitant effect of a common toxic or infective cause. In the diseases enumerated above jaundice is an incidental, and in most instances not a constant, symptom of a well-recognised disease, but in some instances, as Weil's disease (or infectious

¹ Gilbert et Herscher. *Compt. rend. Soc. Biol.*, Paris, 1902, liv, 795.

² Hayem. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1897, 3. s., xiv, 704.

³ Gilbert et Lereboullet. *Gaz. hebdom. de méd.*, Paris, 1902, vii, 889.

jaundice) and acute yellow atrophy, it is one of the most characteristic, if not the most essential, of the clinical features.

(ii) Some of the poisons which give rise to toxæmic jaundice have been already referred to, such as toluylenediamine, phosphorus, snake-bite. In addition, jaundice occasionally follows large doses of chloroform, chloral, coal-tar products such as acetanilide, santonin, filix mas, poisoning by arseniuretted hydrogen, aniline, mushrooms, and even in fatal sulphate of copper poisoning.

(iii) Chronic splenomegalic hæmolytic jaundice is described on p. 537.

General Characters and Distinctions from Obstructive Jaundice.—

Haemo-hepatogenous or toxæmic jaundice is essentially a sign of some underlying infection or intoxication, and is usually subordinate to the constitutional symptoms. The patient suffers comparatively little from the presence of bile in the general circulation, but is definitely and often severely ill from the primary disease or intoxication. The jaundice is, as a rule, slight, though in acute yellow atrophy and icterus gravis it is bright yellow, and the dark-green tint of chronic obstructive jaundice does not occur. There may be manifest toxæmia, as shewn by cutaneous, nasal, gingival, and gastro-intestinal hæmorrhages, and by nervous symptoms. The urine contains less bilirubin than in obstructive jaundice, but, ~~since bile reaches the intestine and is there exposed to putrefactive and fermentative changes, urobilin is formed, absorbed, and excreted in the urine; whereas in obstructive jaundice, when bile is excluded from the~~ bowels, there is no urobilinuria. In both toxæmic and obstructive jaundice bile acids are present in the urine for the first few days, but not after this; the amount of the bile acids found in the urine during these early days is rather less in toxæmic than in obstructive icterus. Hay's sulphur test should be employed in preference to Pettenkofer's test for bile acids. As the result of the general hæmic infection or intoxication there are often changes in the renal epithelium leading to albuminuria.

The faeces contain stercobilin, sometimes even in excess; this is due to increased secretion of bile-pigments (polychromia) as a result of the toxæmia augmenting the supply of hæmoglobin to the liver cells. The motions in toxæmic jaundice thus differ markedly from the clay-coloured dejecta of cases in which, from complete obstruction of the ducts, bile is ~~excluded from the intestines,~~ *only by excretion from the blood vessels*

The course of the disease is more acute, as a rule, than in obstructive icterus, and is not accompanied by the itching of the skin, xanthopsia or yellow vision, and slow pulse which may accompany obstructive jaundice. Signs of constitutional disturbance, such as enlarged spleen, fever and albuminuria, are common, and grave symptoms appear sooner and more frequently than in obstructive jaundice, in which they only occur late or at the termination of long-continued jaundice. In severe cases of haemo-hepatogenous jaundice the "typhoid state," with dry tongue, delirium, coma, and multiple hæmorrhages, may rapidly develop. The important features, therefore, are the want of proportion between

1/ after SALVARSAN¹⁹¹⁰ and

2/ but this has recently been disputed (Brule et Spilliaert)

Brule et Spilliaert. Annales Med., Par., '92'. ix, 577

1. SEI-I-KWAI (med. Journ., Tokyo, 1912, xxxi, 176)

On the other hand ^{sometimes} it appears that
the condition *conditio* dies out in
the fourth generation (Campbell)

Campbell, J. M. H. Guy's Hosp. Rep., 1921, LXXI, 274.

the slight degree of jaundice and the marked constitutional symptoms, and evidence of haemic infection or intoxication.

Chronic Splenomegalic Haemolytic Jaundice.—*Synonyms*: Haemolytic jaundice with splenomegaly; familial splenomegalic cholaemia; chronic simple jaundice with splenomegaly; chronic infective jaundice (Hayem).

Definition.—Chronic jaundice, moderate though varying in degree, accompanied by enlargement of the spleen, but by little or no enlargement of the liver, urobilinuria, absence of bile from the urine (acholuria), and normally coloured faeces. The red blood-corpuscles are characteristically “fragile,” namely, undergo haemolysis in hypotonic salt solutions in an abnormal manner. There is no evidence that the jaundice is obstructive.

Introduction.—The special interest of chronic haemolytic jaundice is that it may prove to be an exception to the general rule that all jaundice is due to obstruction somewhere in the biliary tract; for, as will be seen later, there is some evidence that it is a truly haematogenous jaundice, namely, that the bilirubin is manufactured in the circulation.

History.—In 1885 Murchison¹ described a family, a later generation of which was proved in 1909 to shew this condition (Hutchison and Pantou²). Wilson³ (1890, 1893) reported a family in this country with one necropsy, and in 1900 Minkowski⁴ gave a detailed description of a family with a necropsy in which there was no evidence of biliary obstruction. Little notice was taken of the condition until Chauffard’s⁵ discovery (1907, 1908) of the characteristic fragility of the red blood-corpuscles called forth a copious literature in France. In this country Parkes Weber⁶ and in America Thayer and Morris,⁷ and Tileston and Griffin⁸ have paid special attention to the subject. Chronic haemolytic jaundice may be divided into (a) the hereditary, familial, and congenital, and (b) the acquired forms. The following description will deal with these two forms in common, the differences between them being noted under the “clinical features.”

Etiology.—The hereditary, congenital, and familial forms may shew various combinations, thus the condition may be hereditary and congenital, or hereditary but not congenital; in the same family jaundice may come on after birth in one generation and be congenital in subsequent generations (Benjamin and Sluka⁹). This process of “anticipation” suggests that the morbid process becomes intensified.

¹ Murchison. *Diseases of the Liver*, 3rd edit., p. 481, 1885.

² Hutchison and Pantou. *Quart. Journ. Med.*, Oxford, 1908–9, ii, 452.

³ Wilson, C. *Trans. Clin. Soc.*, Lond., 1890, xxiii, 162; and (with D. Stanley) *Ibid.* 1893, xxvi, 163.

⁴ Minkowski. *Verhandl. d. Congr. f. inn. Med.*, Wiesbaden, 1900, xviii, 316.

⁵ Chauffard. *Semaine méd.*, Paris, 1907, xxvii, 25; 1908, xxviii, 48.

⁶ Weber. *Internat. Clinics*, Phila., 1909, s. 19, ii, 85; *Amer. Journ. Med. Sc.*, Phila., 1909, cxxxviii, 24; (with Dorner) *Lancet*, Lond., 1910, i, 227.

⁷ Thayer and Morris. *Johns Hopkins Hosp. Bull.*, Balt., 1911, xxii, 85.

⁸ Tileston and Griffin. *Am. Journ. Med. Sc.*, Phila., 1910, cxxxix, 847.

⁹ Benjamin und Sluka. *Berlin. klin. Wchnschr.*, 1907, xlv, 1065.

Chronic haemolytic jaundice presents ^{superficial} resemblances to other diseases, such as simple family cholaemia, chronic splenic anaemia of adults, and hypertrophic biliary cirrhosis, especially the metasplenomegalic form, in which the spleen is enlarged first. There are apparently some cases of chronic haemolytic jaundice in which the spleen is not enlarged (A. Pick¹). In Cade's² series there appeared to be some relation between haemolytic jaundice and simple family cholaemia; a man with splenic enlargement and chronic jaundice, whose blood was normal as regards haemolysis, was therefore regarded as the subject of simple family cholaemia; of his seven children three had haemolytic jaundice with splenomegaly, in one this was congenital, in the other two it appeared some years after birth.

Acquired haemolytic jaundice may appear in adult life without apparent cause, or may follow some infection. Brulé³ divided the cases into primary, which arise without any obvious cause or come on during some transient acute disease and persist indefinitely; and secondary cases, which are transient complications of acute infections or of the action of poisons. Hayem⁴ regarded the condition as due to ~~syphilis~~ ^{not congenital} but there is no evidence of this in most of the cases, and the Wassermann reaction has been ~~tried~~ tried in some cases ~~and~~ found to be negative ~~(Weber)~~.

Pathogeny.—The characteristic feature of the blood in chronic haemolytic jaundice is "fragility" of the red blood-corpuscles, which break up with undue facility, and thus provide an increased amount of haemoglobin to form bilirubin. The cause of this fragility is not known, but it has been thought to be due ~~either~~ to inadequacy of the bone marrow or to some "inborn error of metabolism." The haemolysis is not due to a haemolysin in the blood, ~~and has been considered to depend either on the fragility of the corpuscles or on activity of the spleen (Minkowski, Chauffard, Banti).~~ There is little proof that the haemolysis is due to the spleen; the chief arguments are that excessive phagocytic activity in the spleen was described in one case by Vaquez and Giroux,⁵ and that cures have followed splenectomy (*vide* p. 540). ~~There is some evidence, which Thayer and Morris have collected, that bile-pigment can be formed in old haemorrhages in parts of the body other than the liver.~~ It has been suggested that haemoglobin is transformed into bilirubin by a tryptic ferment in the presence of a carbohydrate, such as glycogen or dextrose; and that, though these conditions are usually provided by the liver, the change may be carried out in the tissues.

~~The mechanism by which the jaundice is produced is doubtful; it is~~ not due to inflammation of the small intrahepatic ducts or to viscosity of the bile, for there are no microscopical changes in the minute ducts, and in a patient on whom cholecystotomy had been performed for suspected gall-stone, large quantities of normal and strikingly fluid bile were dis-

¹ Pick, A. *Wien. klin. Wchnschr.*, 1903, xvi, 493.

² Cade. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1908, 3. s., xxv, 421.

³ Brulé. *Thèse de Paris*, 1909, No. 88.

⁴ Hayem. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1908, 3. s., xxv, 122.

⁵ Vaquez et Giroux. *Ibid.*, 1907, 3. s., xxiv, 1184.

Congenital haemolytic jaundice has been associated with congenital spherules (FOURNIER and SOLTRAIN)

s) and derived the haemolytic organ

Portal cirrhosis is said to be a comparatively frequent etiological factor in acquired haemolytic jaundice (Chandler).

1) overactivity of the reticulo-endothelial system, to

1) Though the group of cases of hemolytic jaundice (Chauffard and Troisin)

Medel, ²romane, Abnorme ch
Kinderg Bull Soc med des hop.
1911, 3-5, xxxii 307

Haemolytic jaundice due to
anaerobic *Bacillus perfringens*

Experimentally Whipple and Hooper have shown that ^{in dogs} haemoglobin can be rapidly changed into bile pigment in the circulation ~~without the participation~~ when it is excluded from the blood.

the circulation without the participation of which
the liver, though left in the body, ~~tends to bleed~~, exuded
~~from the~~ ^{Circulation +} ~~was expected~~. This observation led to the conclusion
than endothelial cells - the reticulo-endothelial ~~cells~~
system of ~~Rochoff~~ ^{Rochow} - ~~and especially Kupffer's cells~~
and not the hepatic cells form bilirubin from haemoglobin.
By extirpation of the liver in dogs Rich finds that there is
no transformation of haemoglobin injected into the circulation,
into bile pigment; and that Whipple and Hooper's results were due to activity of Kupffer's cells on the liver.

FOURNIER et JOLTRAIN. Bull. et mém. Soc. méd. des hôp. de Paris, 1913, 3. s., XXXV, 487.

Chalier. Rev. de méd., Par., 1911 (Jubilé du Prof. R. Lépime) 171

Whipple and Hooper. Journ. exper. Med., N.Y., 1913, xvij, 612.

Rich, A.R. Bull. Johns Hopkins Hosp., Baltimore, 1923, XXXIV, 321

For long account see
Folia et Pancreas 1920
Tome XII of Traité de pathologie et de thérapeutique

spleen and lymphatic glands and the
pancreas ~~with~~ ⁱⁿ ~~the~~ ^{the} ~~case~~ ^{case}
The marrow of the long bones shows
the fetal condition

The fragility may intermittent or be
absent in cases of hemolytic
spherocytic jaundice (Chabrol and
Bénard)

no bile salts or / ^

Giffin has collected 4 cases with
hemozytobinuria

Out of Chauffard's 18 cases
7 had these attacks

Chabrol et Bénard. Gaz. des hôp., Paris 1921
Giffin, H. J. Arch. Int. Med., Chicago, 1923, ~~vol.~~ 53, 29
Chauffard. La leucémie bilieuse, p. 65, 1922

charged. There is thus a ^{two} want of evidence that the jaundice is hepatic in origin; and, though it cannot be established as proved, it is possible that the jaundice is haematogenous and due to the formation of bilirubin from haemoglobin in the circulation and tissues. It has, however, been thought that there is an increased secretion of bile by the liver and that the excess runs over into the haemic capillaries in the liver (Haus¹).

Morbid Anatomy.—The bile-ducts both outside and inside the liver are free from any signs of obstruction or inflammation. In 5 out of 6 necropsies on congenital cases, small pigment calculi were found in the gall-bladder (Guizzetti²); these calculi, which were confined to the gall-bladder, could not account for the jaundice, and must be regarded as a complication. The liver cells shew an iron-containing pigment (haemosiderin), which is usually also seen in the kidneys. The spleen has been found to shew engorgement, siderosis, but no fibrosis. In one case phagocytic activity was described (Vaquez and Giroux).

Clinical Features.—In the hereditary, congenital, and familial cases the blood shews characteristic changes. In 1907 Chauffard discovered that the red blood-corpuscles underwent haemolysis in an abnormal manner when exposed to hypotonic solutions of saline solution; normally haemolysis of the red blood-corpuscles begins in 0.42 per cent NaCl solution and is complete in 0.3 per cent; whilst in haemolytic jaundice it begins at 0.6 per cent and is complete at 0.42 per cent; this is spoken of as fragility. The red blood-corpuscles are smaller than normal, 6μ in diameter instead of the normal 7.5μ , and on appropriate staining shew basophil granules, especially at the periphery, and usually well-marked polychromatophilia. There is generally moderate anaemia; but polycythaemia has been described in two cases (Guinon, Rist, and Simon³; Mosse⁴); the colour index is less than one; the serum contains bilirubin, but ~~not~~ free haemoglobin, ~~and~~ is hypertonic, ~~and contains a diminished amount of~~ ^{cholesterin.}

The urine is high-coloured, usually contains urobilin, but is free from bile, though in some cases bile appears temporarily in the urine during ^{and} ~~exacerbations~~ ^{complications}. The faeces are normal in colour except in the exacerbations, when they are sometimes pale. The jaundice varies and may almost disappear; it becomes more marked after excitement, exposure to cold, and excessive exertion. There is remarkable freedom from the usual symptoms of chronic jaundice, such as itching, slow pulse, and from xanthoma and clubbing of the fingers. The condition is compatible with long life, up to 70, and there is no arrest of growth or development. The ~~only~~ ^{most} symptoms of importance ~~are~~ ^{are} the occurrence in some cases of attacks of abdominal pain imitating biliary colic, and probably connected with the presence of pigment calculi in the gall-bladder; the attacks are accompanied by a raised temperature, drowsiness, and increase in the jaundice, and are possibly due to infection. The spleen is nearly

¹ Haus. *Norsk Mag. f. Laegevidensk.*, Christiania, 1910, lxxi, 1277.

² Guizzetti. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1912, lii, 15.

³ Guinon, Rist, et Simon. *Bull. et mêm. Soc. méd. des hôp. de Paris*, 1904, 3. s., xxi, 786.

⁴ Mosse. *Deutsche med. Wchnschr.*, 1907, xxxiii, 2175.

appears

frequently shew

due to the long continued haemolysis

cholesterin.

of exacerbation of jaundice is anaemia which runs parallel, and

The spleen is nearly always enlarged 7 cm. in diameter the acquired form; it increases in size and becomes tender during the

acute stage during exacerbation

In the acquired form, ^{which most commonly attacks young females,} the degree of anaemia is more marked and the jaundice less pronounced than in the congenital form, ~~in fact~~ the blood may resemble that of pernicious anaemia, with a high colour-index and nucleated reds with megaloblasts, but there is leucocytosis with myelocytes and eosinophilia. The fragility of the reds is slight when tested with unwashed corpuscles, ~~and thus contrasts with the congenital form in which the fragility is marked and the anaemia moderate.~~ Another special feature of the blood in the acquired cases is its auto-agglutinative power. In contrast to the congenital form, the patients are definitely ill and suffer from anaemia as well as from attacks of febrile biliary colic. The condition may imitate pernicious anaemia or gall-stones. As the result of febrile attacks the anaemia may advance very rapidly.

Prognosis.—In the hereditary, congenital, and familial forms the outlook as regards life is extremely good, in fact the subjects of the disorder are not ill, but they never become absolutely normal. In the acquired cases, on the other hand, a cure has resulted.

Diagnosis.—The characteristic fragility of the red blood-corpuscles distinguishes the condition from other forms of jaundice, including gall-stones and pernicious anaemia with icterus, in which the resistance of the red blood-corpuscles to haemolysis is increased. By this means the diagnosis of cases in which the jaundice is slight or temporarily absent, from splenic anaemia can also be made.

Treatment.—The subjects of the hereditary, congenital, and familial forms should lead a protected life, so as to avoid cold, over-exertion, and excitement, which lead to exacerbations. The attacks of abdominal pain require symptomatic remedies, but otherwise treatment is hardly necessary. If anaemia is prominent, iron should be given. In the more severe examples of the acquired form rest in bed and iron are indicated; arsenic is not of any use. Simple drainage of the gall-bladder, which would be reasonable if there was any evidence of biliary infection, has seldom been carried out; in one case jaundice returned after closure of the fistula (Chauffard and Troisier¹). Splenectomy ~~has been reported to have been followed by a cure (Micheli,² Banti³).~~ The diet should be simple and nourishing. Constipation and intestinal putrefaction should be prevented by purgatives, guaiacol, or calomel $\frac{1}{20}$ gr. t.d.

OBSTRUCTIVE JAUNDICE

Signs.—*Jaundice* appears first in the conjunctiva, where it can be well seen by drawing the lower eyelid down, then successively on the face, neck, body, and extremities. The "whites" of the eyes are the first part to be stained. The masses of fat (pingueculae) often present under the conjunctiva frequently have a slightly yellow colour and may lead to an erroneous diagnosis of jaundice. Slight icterus is more readily

¹ Chauffard et Troisier. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1908, xxv, 411.

² Micheli. *Wien. klin. Wochenschr.*, 1911, xxiv, 1269.

³ Banti. *Pediatrica*, Roma, 1911, xviii (sec. part.), 1558.

1) though its onset may be sudden.

but it occurs with washed red cells. The red cells are larger than normal (Widal, Abramson and Brulé)

In simple family cholaemia there is no anaemia, the red cells do not show fragility and the jaundice is hepatic in origin.

In ~~the~~ two congenital cases great benefit followed exposure of the spleen to x-rays (Parrisot and Heully) is the recognized method of relief, and in the majority of cases the jaundice rapidly disappears, but the fragility of the red blood cells is unchanged. The operation mortality in 1921 among 93 cases was about 5 per cent.

Benefit has been reported from a diet rich in cholesterol (PARRISOT and HEULLY). (NORRIS and MacMillan)

PARRISOT et HEULLY. Gaz. des hôp. Paris, 1913, LXXXVI, 277

PARRISOT et HEULLY. Bull. et mém. Soc. Méd. des hôp. de Paris, 1912, 3. s., XXXIV, 527.

~~Wright. Proc. Roy. Soc. Med., 1900, vi (Clin. Sect.) 80~~

~~Thurfield. Ibid.~~

~~Abrahamson. Semaine méd. Paris, 1910, 217~~

NORRIS, G. W. and Mac Millan, T. M. Bull. AYER Clin. Lab. Penn. Hosp., 1924, p. 44.

Craig | 1

Neurodermatitis, especially
around the eye, resembling
that in Graves disease, may
occur in chronic obstructive
jaundice

Craig, J. Brit. med. Journ., 1925, i, 453.

detected in a fair-skinned patient than in one of a dark complexion, in whom the skin is often somewhat sallow. It should also be remembered that jaundice is easily overlooked in artificial light. The mucous membrane of the lips and palate shews the icteric tint almost as soon as in the conjunctiva. In prolonged jaundice in infants the teeth have been found to be green (Thursfield,¹ Langmead²). When jaundice has existed for a long time, the bile-pigment in the skin turns of a dark-green colour

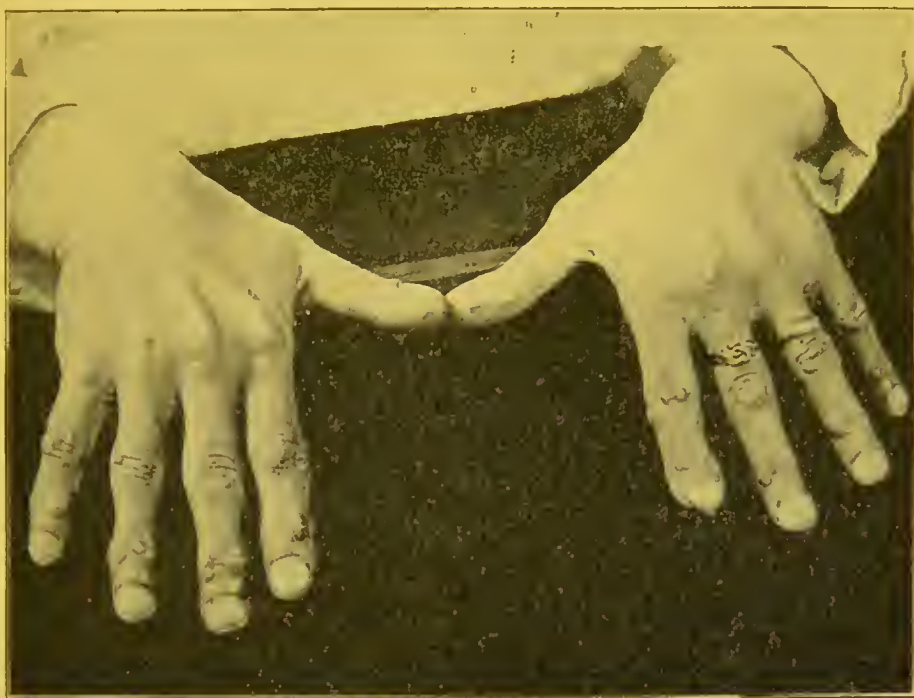


FIG. 78.—Xanthoma tuberosum multiplex in a Jewess who had had jaundice for fourteen years; the liver and spleen were enlarged (Dr. Graham Steell's case).

(biliverdin), and the condition is often spoken of as "black jaundice." In rare instances areas of leucodermia have appeared in jaundice due to malignant disease (Warthin,³ Rolleston⁴); in Warthin's case the medullas of the suprarenals were infiltrated with growth.

In chronic jaundice, usually of some years' duration, multiple xanthoma, xanthelasma, or vitiligoidea may occur. The relation between chronic icterus and this rare skin disease is uncertain, for xanthoma may occur in the absence of jaundice, and it is seen in a small percentage only of the cases of chronic jaundice. According to Chauffard⁵ xanthoma is a local deposit ("tophus") of cholesterol due to excess of cholesterol in the blood. There are two forms: in flat patches and nodular areas. It may be very painful. The plane or flat form may

¹ Thursfield. *Proc. Roy. Soc. Med.*, Lond., 1912, v (Sect. Dis. Child.), 147.

² Langmead. *Ibid.*, 148.

³ Warthin. *Phila. Med. Journ.*, 1900, vi, 38.

⁴ Rolleston. *Proc. Roy. Soc. Med.*, Lond., 1910, iii (Clin. Sect.), 195.

⁵ Chauffard. *Rev. de méd.*, Paris, 1911, xxxi (Jubilé du Prof. R. Lépine), 177.

also occur on mucous membranes. In chronic jaundice there is a tendency to the formation of stigmata, or spider angiomas, on the skin of the face and elsewhere. As the jaundice passes off, the angiomas may also recede (Osler). When, as the result of complete biliary obstruction or from other causes, the protective function of the liver fails, and toxins, manufactured in the alimentary canal, pass into the circulation and give rise to cholaemia, cutaneous and mucous haemorrhages, such as epistaxis and melaena, occur.

The *urine* is acid, and is somewhat diminished in amount. It becomes bile-stained before the conjunctiva or the skin; as much as twenty-four hours may elapse between the appearance of bile in the urine and in the conjunctiva. The colour of the urine varies from an intense yellow, to brown, olive, or a very dark brown. In rare instances in which there is a considerable amount of biliverdin, bilirubin, and other bile-pigments, the urine may appear black (Garrod¹). When shaken up, the froth becomes yellow. The colour must be distinguished from that in urobilinuria, haematuria, melanuria, and the alterations due to rhubarb, chrysophanic acid, senna, and santolin, by Gmelin's test for bile-pigment.

Occasionally, especially during convalescence, in obstructive jaundice the urine contains no bilirubin, although the skin is still jaundiced. When bile is completely excluded from the bowel, there is no urobilin in the urine; ~~but~~ when the obstruction is incomplete and allows some bile to escape into the duodenum, urobilinuria may appear, urobilin being manufactured from bilirubin in the intestine by microbic activity. Bile salts are present in the urine for the first few days of jaundice, and then disappear; the same holds good in toxaemic jaundice; but the quantity of bile salts in the urine is larger in obstructive than in toxaemic jaundice. The disappearance of bile salts from the urine probably depends on their diminished production in all forms of icterus. In marked jaundice there may be mucus (nucleo-albumin). As a result of the bacterial decomposition of proteins (putrefaction) in the alimentary tract the ethereal sulphates are increased and a considerable amount of indican may be found. It must, however, be remembered that aromatic drugs such as creosote and salol, which are frequently given to control flatulence, are said to increase the ethereal sulphates in the urine (Herter²).

When, in the late stages of obstructive jaundice, cholaemia has supervened, the renal epithelium may suffer and albuminuria occur. Casts, if looked for, are almost always present; they depend on the jaundice, and are not necessarily accompanied by albuminuria. Experimental ligature of the bile-duct has been found to give rise to casts in the urine without albuminuria (Wallerstein³). In about 40 per cent of urines containing bile there is reduction of Fehling's solution due to the presence of glycuronic acid (Cambridge⁴).

¹ Garrod. *Practitioner*, Lond., 1904, lxxii, 386.

² Herter. *Lectures on Chemical Pathology*, p. 205, 1902.

³ Wallerstein. *Berlin. klin. Wchnschr.*, 1902, xxxix, 310.

⁴ Cambridge. *Treatment*, Lond., 1905-6, ix, 649.

has
usually
containing
flat

and
flat

3 But recently evidence has been brought forward to show that even with complete obstruction of the common duct bile pigments or urobilin (which is formed in the liver & not in the intestine) are excreted by the blood vessels into the intestine and that the faeces contain stercobilin and urobilin. (BRULÉ and SPILLIAERT)

BRULÉ et SPILLIAERT. Ann. de méd. Par., 1921, 4, 577

The Faeces.—There is usually constipation, and the motions are bulky, of low specific gravity, and often extremely offensive, mainly from the presence of fatty acids. In the absence of bile the faeces are pale and are devoid of hydrobilirubin; the “clay-coloured” appearance being partly due to the absence of the pigment and partly to an excess of finely divided fat and bubbles of gas. The presence of fat in excess probably interferes with absorption of proteins and favours fermentation. When bile is excluded from the bowel the undigested fat may rise from the normal 7 to 10 per cent to 55 or 78·5 per cent (Müller¹). When obstruction is not complete, bile enters the bowel and the faeces are of a fairly normal colour. This may occur when one of the two hepatic ducts is obstructed, or when a “floating” gall-stone in the common duct allows some bile to escape into the duodenum.

Other Secretions.—There has been a good deal of discussion and discrepancy of opinion about the condition of the various secretions in jaundice. The majority, such as the saliva, the mucus of the mouth and alimentary canal, are not bile-stained. The perspiration is usually free from bile, but it may be present in the secretions of the axilla. Tears and women’s milk are more often free from bile than jaundiced. Although the bile-pigments do not appear in the saliva, the salivary glands themselves, like other organs, are deeply bile-stained. The cerebrospinal fluid is free from bile pigment; but in certain pathological conditions it may give Gmelin’s test for bilirubin; thus Gilbert and Castaigne² obtained a positive reaction in 3 jaundiced patients with nervous diseases; in Mosny and Javal’s³ case there was a sarcomatous growth in the dura mater and the cerebrospinal fluid contained bile, and it is bile-stained in the “Kernicterus” of infants dying with jaundice. In inflammatory conditions the pathological secretions and exudations become icteric, as shewn by pneumonic sputum, pleural and peritoneal effusions, and saliva in mercurial salivation.

Circulatory System.—In the absence of pain and fever the pulse tends to be slow. This is generally true, but in 1902 Mackenzie⁴ had never met with a slow pulse in jaundice, and Thomson⁵ states that it does not occur in children. It is especially in catarrhal and recent jaundice that slowing of the heart’s beat is most marked. It has been ascribed to the inhibitory action of bile salts on the cardiac ganglia, on the myocardium, or to stimulation of the inhibitory fibres of the vagus; for bile acids pass into the blood in the early stage of jaundice, but are produced in very small quantities when jaundice is established. King and Stewart,⁶ however, have shewn that the slow pulse is due to the bile-pigments. The pulse is ~~frequently observed to vary~~ very considerably with position; *often varies* sitting up may increase the pulse-rate by, twenty beats. The arterial

¹ Müller. *Ztschr. f. klin. Med.*, Berl., 1887, xii, 45.

² Gilbert et Castaigne. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1908, 3. s., xxv, 598.

³ Mosny et Javal. *Ibid.*, 1909, 3. s., xxviii, 280.

⁴ Mackenzie, J. *The Study of the Pulse*, p. 134, 1902.

⁵ Thomson, J. *Clinical Examination and Treatment of Sick Children*, p. 235, 1908.

⁶ King and Stewart. *Journ. Exper. Med.*, N.Y., 1909, ix, 673.

blood pressure is low. Experimental injection of bile into the jugular vein of rabbits has produced a fall of blood-pressure, and rendered the inhibitory action of the vagus more marked (Meltzer and Salant¹). From muscular incompetence a mitral systolic murmur may become audible, and from increased pressure in the pulmonary circulation, due to this cause or possibly to reflex constriction of the pulmonary vessels referred from the bile-ducts, the pulmonary second sound becomes accentuated.

The blood-serum is stained of a greenish-yellow tint. The specific gravity of the blood as a whole is increased, but that of the serum is unaffected. The coagulation time is prolonged. The blood may take fifteen to twenty minutes to coagulate instead of the normal four minutes (Osler²). In severe cases the alkalinity of the blood has been found to be diminished.▲

There is very little anaemia except in severe cases; this is rather curious, inasmuch as considerable haemolysis from the action of the bile acids might naturally have been expected. The resistance of the red blood-corpuscles to haemolysis by saponin is greatly diminished (M'Neil³), but to hypotonic salt solution it is increased, and, according to Chauffard,⁴ the corpuscles are increased in size; whereas in haemolytic jaundice they break up more readily in hypotonic salt solution, and are smaller than in health. The plasma in obstructive jaundice is hypertonic (v. Limbeck⁵). In advanced obstructive jaundice with cholaemia granular degeneration of the red blood-corpuscles is a prominent feature. In cholaemia there is usually leucocytosis. In jaundice of no great intensity and without grave toxæmic symptoms leucocytosis does not occur unless there is some other cause, such as inflammation or suppuration.

A. S. Grünbaum,⁶ in 1896, pointed out that the undiluted blood-serum of jaundiced patients in many cases agglutinated typhoid bacilli. But in most cases dilution of the serum is followed by such a marked falling off in the agglutinative power that there is no reason to diagnose typhoidal infection. In some cases of jaundice the serum, even when highly diluted, agglutinates typhoid bacilli in such a manner as to lead to the conclusions that there has been an attack of typhoid fever, that the patients are typhoid carriers, or that bacteria closely related to the *B. typhosus* give rise to a group agglutination reaction (Christian⁷).

The *respiration* is usually normal, but the rate may be slowed. The *temperature*, like the functions of the body generally, is depressed. This is probably due to the action of toxins on the tissues, and also to the diminished intake of food and assimilation. Fever, when present, is either due to the cause responsible for the jaundice, as hepatic abscess,

¹ Meltzer and Salant. *Journ. Exper. Med.*, N.Y., 1905, vii, 280.

² Osler, W. *Johns Hopkins Hosp. Bull.*, Balt., 1901, xii, 264.

³ M'Neil. *Journ. Path. and Bacteriol.*, Cambridge, 1911, xv, 56.

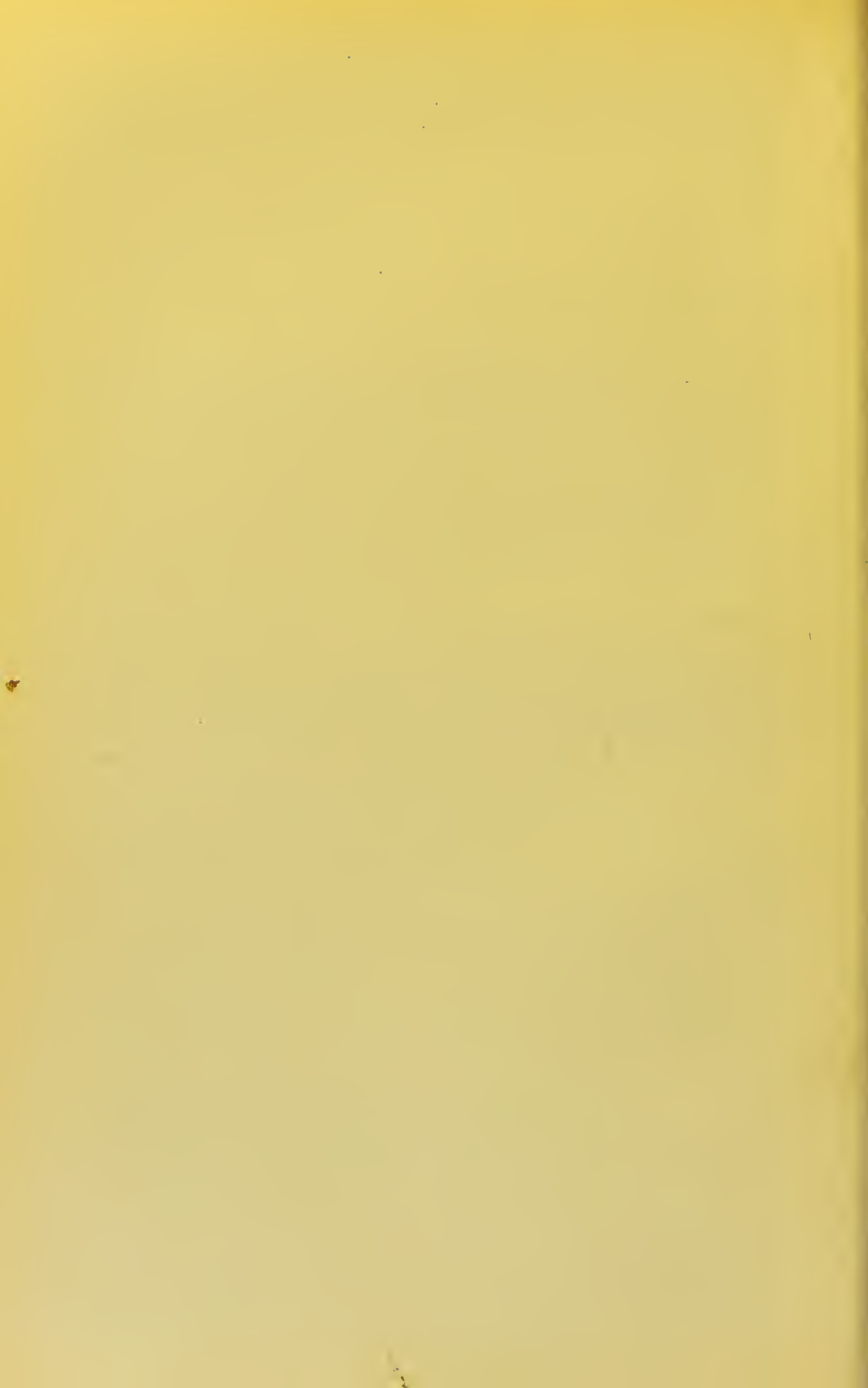
⁴ Chauffard. *Semaine méd.*, Paris, 1908, xxviii, 48.

⁵ von Limbeck. *Clinical Pathology of the Blood*, p. 316, Engl. Transl., Lond., 1901.

⁶ Grünbaum, A. S. *Lancet*, Lond., 1896, ii, 806.

⁷ Christian. *Boston Med. and Surg. Journ.*, 1907, clvi, 536.

The amount of cholesterol^{of} is increased. When bile salts do not enter the intestine.
the blood serum does not show the haemacoma^{or granules of fat}, normally present after a meal
containing fat



gumma, or cirrhosis, or is the result of some complication, such as cholangitis in gall-stone obstruction.

The *liver* is often enlarged from damming-up of the bile, and may be tender. In malignant disease and in cirrhosis its surface may be knobby or irregular.

Enlargement of the Gall-bladder.—In chronic jaundice due to gall-stones the gall-bladder is collapsed from previous cholecystitis, whilst in cases of malignant disease pressing on the common bile-duct the gall-bladder forms a tense, pear-shaped tumour. If a calculus be impacted in the cystic duct, the gall-bladder may be distended with mucus, and occasionally contains numerous calculi; these are exceptions to the general rule enunciated by Courvoisier that in jaundice due to gall-stones the gall-bladder is collapsed, and that in jaundice due to malignant disease it is dilated.

The *spleen* is usually not enlarged, but if it is, it points to biliary cirrhosis, some infective or toxic process, such as Weil's disease or infective jaundice, to syphilis, or to that extremely rare condition, alveolar hydatid.

Symptoms.—Apart from the independent effects of underlying diseases, the symptoms accompanying jaundice are due partly to the presence of bile in the circulation, which acts as a depressant, partly to a secondary toxæmia produced by the failure of the liver to perform its important protective functions of stopping poisons brought to it from the alimentary canal, and partly to the absence of bile from the alimentary canal. These distinctions in the causation of the symptoms must not be pressed too far, but it will be convenient to consider the symptoms under the following heads :—

Symptoms due to Bile in the Circulation.—The normal constituents of bile, the bile-salts, bile-pigments, and cholesterin, must be considered from the point of view of their toxic action on the tissues of the body.

The bile-salts exert a well-marked haemolytic action on red blood-corpuscles outside the body, but it is plain that they are not present in the blood in sufficient amounts in jaundice to produce haemolysis. If haemolysis due to this cause occurred, there should be marked anaemia and escape of blood-pigment in the urine in obstructive jaundice. Neither of these events occurs. The absence of anaemia and haemoglobinuria and the fact that bile-salts are only found in the urine during the first few days of jaundice shew that the production of bile-salts by the liver cells is inhibited during jaundice. The toxic effects of the bile-salts are slight compared with what might naturally have been expected. Slowing of the pulse and dilatation of the peripheral vessels have been thought to be thus caused. The headache and mental depression may in part be due to a similar toxic effect on the brain. Experimentally Meltzer and Salant¹ find that bile contains tetanic and depressing elements which usually neutralise each other. Stagnant bile, as in the gall-bladder,

¹ Meltzer and Salant. *Journ. Exper. Med.*, N.Y., 1905, vii, 280.

invariably produces coma and paralysis. Bile-salts contain the tetanic element in less amount than the whole bile.

Bilirubin was thought by Bouchard to be ten times more toxic than bile-salts, and the comparative immunity from severe symptoms in ordinary jaundice was explained by the consideration that much of this pigment was fixed in the skin and other jaundiced tissues. Gilbert and Herscher¹ find that the amount of bilirubin in the blood-serum in obstructive jaundice does not, so long as the kidneys are healthy, exceed the proportion of 1 gram in 900 c.c. of serum. They suggest that there is an excretory mechanism by which accumulation of bilirubin above this point is prevented. It appears, however, that bilirubin is a comparatively feeble poison; the subjective symptoms which have been referred to it are xanthopsia and pruritus.

Yellow vision, or xanthopsia, has been explained as the result of the retina and media having become so infiltrated with bilirubin that the blue and violet rays are absorbed. As a result, the patient suffers from blue blindness. There is a want of relation between the degree of jaundice and yellow vision; it may be absent in advanced icterus and present when it is slight; it is therefore probably due to toxic disturbance of the retina. Yellow vision is seldom a source of sufficient annoyance to lead to a definite complaint on the patient's part, but on inquiry it is not infrequently found. The yellow vision which follows the administration of santonin is more noticeable.

Pruritus, or itching of the skin without any local lesion, ~~was estimated by Frerichs² to occur in about 20 per cent of the cases of jaundice.~~ It is often stated that the irritation of the sensory nerves of the skin is due to the constituents of the bile, especially the bile-salts. But sometimes the itching is independent of jaundice, and may appear weeks before icterus, disappear when the jaundice comes out, or persist after jaundice has gone. Graves³ reported a case of pruritus which began two months before the onset of jaundice and subsided with the onset of jaundice. I have seen a case of most obstinate itching in a woman, without any jaundice, in whom calculi were subsequently removed from the common duct. Riesman⁴ refers to the prompt disappearance of pruritus in some cases after drainage of the gall-bladder. Cabot⁵ mentions a case with two attacks of jaundice due to gall-stones; one attack was accompanied by severe pruritus, the other was not. The cause of the pruritus is not known, but these considerations suggest that it is a concomitant, rather than a result, of jaundice. It may be due to hepatic inadequacy and to the presence of irritating poisons in the circulation. Robson⁶ specially connects pancreatic disease with severe itching. It has also been suggested that it depends on the dry and ill-nourished condition of the skin. Accord-

(c)

¹ Gilbert et Herscher. *Compt. rend. Soc. Biol.*, Paris, 1906, lix, 208.

² Frerichs. *Diseases of the Liver*, Transl. New Syd. Soc., 1861, ii, 107.

³ Graves. *Clinical Lectures*, New Syd. Soc., 1884, ii, 296.

⁴ Riesman. *Am. Med.*, 1907, N.S., ii, 77.

⁵ Cabot. *Differential Diagnosis*, p. 719, 1912.

⁶ Robson. *Surg., Gynec., and Obst.*, Chicago, 1908, vi, 29.

1/12 said to occur in from 20 (Furichs) to 50 per cent (Cabot)

Cabot. Differential Diagnosis, p 707, 1911

and even suggest
suicide. / ^

ing to Ricsman pre-icteric pruritus is suggestive, though not pathognomonic, of malignant disease. Itching is said not to occur in young children. The itching is usually associated with well-developed jaundice. The irritation may be excessive, ~~and~~ prevent sleep; the scratching may induce traumatic eczema. Urticaria and lichen are sometimes seen on a jaundiced skin. Urticaria has a very curious appearance, the bile-stained exudation making the bullae look much more jaundiced than the surrounding skin.

Cholesterin was thought by Flint¹ to cause the grave nervous symptoms occurring late in the course of obstructive jaundice, and the term cholester-aemia was employed in the sense that cholaemia often is now. There is no satisfactory evidence that cholesterin is toxic. It is true that experimental injection of cholesterin into the body has been followed by bad results. But these were probably either mechanical and due to obstruction of small blood-vessels, or caused by the glycerin in which the cholesterin was suspended (Herter²). Xanthoma and gall-stones have been ascribed to excess of cholesterin in the blood (Chauffard³).

Symptoms due to the Presence of Poisons other than Bile in the Circulation.—Owing to the failure of the liver to stop poisons received from the alimentary canal, auto-intoxication results, and if the kidneys do not compensate for this by free diuresis, a toxæmic condition, analogous to that of uraemia, results. The increased fermentation and putrefaction consequent on the exclusion of bile from the bowel render the process of auto-intoxication of considerable importance. In a minor degree mental depression, incapacity for continued mental effort, drowsiness, headache, and general debility are the results of this hepatic toxæmia, while in more marked degrees there may be delirium, somnolence, and coma. A bitter taste in the mouth is common, although the saliva does not contain bile-pigment, and may be due to toxic ~~bodies~~, which, owing to hepatic insufficiency, have escaped into the general circulation, and so into the saliva. ~~There is often considerably impairment of appetite~~ especially for fatty food.

The tendency to haemorrhage in chronic obstructive jaundice is of great importance when any surgical operation has to be performed, as fatal haemorrhage may result. Cerebral haemorrhage is very rare; Mayo Robson⁴ mentions a case; I have seen one. Haemorrhages into the skin are common, and epistaxis sometimes causes anxiety. The frequent oozing from the gums is accompanied by offensive breath. The coagulation time of the blood in chronic jaundice is much prolonged; instead of four it may be fifteen or twenty minutes (Osler⁵). This blood change may be due to hepatic insufficiency and diminution of the fibrinogen in the blood, or to the failure of the liver to stop poisons and bodies allied to peptones absorbed from the alimentary canal. The

¹ Austin Flint, Jr. *Am. Journ. Med. Sc.*, Phila., 1862, xliii, 305.

² Herter. *Lectures on Chemical Pathology*, 1902, p. 331.

³ Chauffard. *Rev. de méd.*, Paris, 1911, xxxi (Jubilé du Prof. Lépine), 177.

⁴ Robson and Cammidge. *The Pancreas, its Surgery and Pathology*, p. 317, 1907.

⁵ Osler, W. *Johns Hopkins Hosp. Bull.*, Balt., 1901, xii, 264.

poisons would damage the blood-vessels, while the peptone-like bodies would interfere with the coagulation of the blood. Mayo Robson,¹ however, suggested that the haemorrhagic tendency is pancreatic in origin, and that it may depend on a diminution of lime salts in the blood due to a profuse excretion of lime salts in the urine in pancreatitis.

In experimental obstructive jaundice in dogs it has been found that the calcium content of the blood is not diminished, but that the calcium salts are fixed to the bile-pigment; this fixation of the calcium salts protects the body against the toxic action of bile-pigment, but it also disturbs the coagulation time of the blood, and plays a part in producing slow pulse (King, Bigelow, Pearce²).

Symptoms due to the Absence of Bile from the Intestinal Tract.—Constipation is common, and is usually explained by the absence of the natural purgative, bile. As micro-organisms grow freely in bile, it cannot be regarded as an antiseptic, but flatulence is frequent, and the absorption of the poisonous bodies produced in the intestine may account for headache, mental depression, and other symptoms. The interference with the absorption of fat leads to considerable loss of weight. The finely diffused fat probably favours fermentative changes in the bowel in addition to interfering with absorption of the other food elements.

DIAGNOSIS OF JAUNDICE

As has already been pointed out, jaundice may be overlooked altogether if the patient is seen only by yellow artificial light, such as gas or candle illumination. No serious difficulty should arise in distinguishing jaundice from other pigmentary changes in the skin. The yellow colour of patients with slight icterus is hardly likely to be confused with the bronzing of sunburn, with the natural hue of the yellow-skinned races, or with the tint of the skin in the advanced cachexia of malignant disease; but should any question arise, examination of the conjunctivae and of the urine, or of blood-serum obtained from a blister, for the presence of bile-pigment will quickly settle the matter. ~~In patients who have absorbed picric acid the skin, conjunctiva, and urine often become yellow, but the urine does not give the reaction of bile-pigment.~~ The dark-green colour of the skin in "black" jaundice of long-continued biliary obstruction might conceivably be confused with the pigmentation of the skin in Addison's disease, haemochromatosis, malarial melanaemia, argyria, etc., but here again examination of the conjunctivae, urine, and blood-serum will prevent error.

The past effects of severe jaundice may cause some difficulty, but further investigation and the history of the case should make matters clear.

¹ Robson, Mayo. *Brit. Med. Journ.*, 1901, i, 1131; and *Lancet*, Lond., 1904, i, 770.

² King, Bigelow, Pearce. *Journ. Exper. Med.*, N.Y., 1911, xiv, 159.

Xanthosis of the skin due to a lutein-like body and .
seen in cases of diabetes does not affect the sclerotic (Wol-
stor does the yellowish color especially of the palms and
soles due to Carotinemia resulting from the consumption
of carrots and Sarsaparilla (Hess and Myers)

Weber, F. P. Brit. Journ. Dermat. and Syph. London, 1921, XXXIII, 123

Hess and Myers. Journ. Am. Med. Assoc., Chicago, 1919, LXXIII, 1743

Five or 10 grains of
 picric acid taken
 internally stains the
 skin yellow for a week
 or two, but the urine
 gives the reaction for
~~picric~~ acids and not
 for bile (Pollock). An
 epidemic of this
 condition has been
 reported*. In Carotinaemia,
 due to carotin the pigment
 in carrots, the skin but
 not the conjunctivae, is
 stained yellow (Head
 and Johnson). A similar
 condition, due to the excessive
 consumption of oranges
 has been termed
 aurantiiasis (Miyaka).

Conjunctiva
 and
 (which is porphyrinated)
 or for a more
 advanced
 derivatives
 triaminophenol,
 picramic

Pollock. Louv. Roy. Army Med. Corps.
 1911, XVI, 60

* Garner, Vassier, et Roussille
Arch. de med. et pharm. méd.
 1914, LXIII, 361.

Head and Johnson. Arch. int. Med., Chicag.
 1921, XXVIII, 261

Miyaka, I. Arch. f. Dermat. u. Syphil., 1924, CXIV, 184

In a case reported by Cavafy¹ a man aged twenty-nine, who had had syphilis, had abnormal pigmentation and itching of the skin left behind by jaundice eight years previously. A committee reported that it was leucodermia.

Feigned Jaundice.—The skin may be ~~coloured~~ yellow by malingeringers ^{^/ painted} in order to escape ~~active~~ work or punishment; saffron and turmeric may be ^{applied} employed for this purpose.² The fraud should be readily detected by the absence of bile-pigment from the conjunctivae and urine. If an attempt is made to darken the urine by taking rhubarb or santolin, Gmelin's reaction with nitric acid is absent, and the addition of alkalis turns the urine red instead of brown.

Differential Diagnosis of Jaundice due to various Causes.—Since the distinction between obstructive jaundice and toxæmic (or hæmo-hepatogenous) jaundice has already been considered (p. 536), it is now only necessary to refer to the differential diagnosis and the various causes of obstructive jaundice. The numerous causes of obstructive jaundice may be grouped into three classes:—

(1) Where the obstruction is inside the lumen of the bile-duets, such as a gall-stone or parasites. (2) Where the obstruction depends on changes originating in the walls of the larger bile-duets, *e.g.* catarrhal cholangitis. (3) Where obstruction is produced by processes arising outside the larger duets. Thus, tumours or adhesions may mechanically compress the duets. Malignant tumours may either merely compress or may actually invade the duets; the former is more frequent.

I. Jaundice due to Obstruction inside the Lumen of the Duets ^{^/ is} ~~These causes of obstructive jaundice are~~ considered elsewhere. (a) Gall-stones are described on p. 709. It is possible that inspissated mucus may obstruct the duets, but the cause of the excessive amount of mucus is inflammation of the duets and gall-bladder and need not be separately described here. Inflammation of the minute intrahepatic duets occurs in toxæmic jaundice, in biliary cirrhosis (p. 315), and possibly in simple family cholaemia (*vide* p. 40).

(b) *Parasites* may gain access to the duets and mechanically occlude the lumen. A hydatid cyst may discharge into the duets, and, as a result, pieces of membrane or daughter cysts may block the duets and give rise to biliary colic, jaundice, and often to infective cholangitis. The subject is considered at length on p. 418.

Round-worms (*Ascaris lumbricoides*) may enter the common bile-duet from the duodenum and give rise to jaundice. Of this rare condition Mertens³ collected 48 examples. *Fasciola hepatica* (*Distomum hepaticum*), the liver fluke so fatal to sheep, has been found in the duets of the human liver, as have, in rare instances, *Opisthorchis sinensis* and *Opisthorchis novorei*. In these cases the diagnosis depends on the recognition of the worms or their ova in the faeces (*vide* p. 682).

(c) As pathological curiosities reference may be made to the presence

¹ Cavafy, J. *Trans. Path. Soc., Lond.*, 1881, xxxii, 258.

² Legg, Wickham. *Bile, Jaundice, and Bilious Diseases*, p. 375, 1880.

³ Mertens. *Deutsche med. Wochenschr.*, 1898, xxiv, 358.

of *foreign bodies*, such as fruit-seeds, small cherry-stones, and needles, in the bile-ducts (Graham¹), but suspicion as to the nature of such foreign bodies must always arise unless the absence of the constituents of gall-stones has been definitely proved.

(d) In most exceptional instances *tumours* may extend along the lumen of the common bile-duct and occlude it without necessarily invading the walls of the duct except at the point where they originate or gain entrance into the lumen of the duct. This has been observed in primary malignant disease of the gall-bladder—a cylinder of growth projecting into the common bile-duct (Bohnstedt²)—and in primary carcinoma of the liver (Gilbert and Claude³).

II. Jaundice due to Changes in the Walls of the larger Ducts.—

(a) *Catarrhal jaundice* due to inflammatory swelling of the mucous membrane of the common bile-duct, either inside the biliary papilla or in the lower part of the duct, is described elsewhere (p. 663). It is preceded by vomiting and diarrhoea, is usually of short duration, and is not accompanied by the splenic enlargement, albuminuria, and fever seen in severe infectious jaundice.

(b) *The infective and suppurative forms of cholangitis* are usually associated with gall-stones or rupture of a hydatid cyst into the ducts, but comparatively often complicate the rare condition of malignant disease of the duodenum involving the papilla. Infective cholangitis presents the symptoms of intermittent hepatic fever (*vide* p. 759), while in suppurative cholangitis (*vide* p. 671), in which, however, jaundice is by no means constant, the clinical picture is that of intrahepatic suppuration, and may closely resemble suppurative pyelephlebitis. Jaundice in the roseolous stage of syphilis may possibly be due to a change, comparable to the cutaneous rash, in the bile-ducts (*vide* p. 349).

(c) *Simple stricture* of the large bile-ducts may be congenital (*vide* p. 649) or acquired (*vide* p. 661). Apart from the cystic duct, stricture of which does not give rise to jaundice, simple stricture of the ducts, such as might conceivably follow cicatrisation of an ulcer set up by a gall-stone, is extremely rare. Hence jaundice occurring some time after biliary colic is more likely to be due either to fresh gall-stone impaction or to malignant disease than to cicatricial stricture.

(d) *Primary tumours of the ducts* may be carcinomatous, or in rare instances innocent; the malignant growths (*vide* p. 689) occlude the lumen and give rise to deep, progressive jaundice and usually to enlargement of the gall-bladder. Innocent tumours, such as a papilloma, are really curiosities (*vide* p. 687). Fagge⁴ described xanthoma on the mucous membrane of the ducts, but it is doubtful if this is the cause of the jaundice.

(e) *Spasm* of the muscular coats of the ducts seems a reasonable

¹ Graham, J. E. Loomis and Thompson's *System of Medicine*, iii, 428.

² Bohnstedt, quoted by Devic et Gallavardin. *Rev. de méd.*, Paris, 1901, xxi, 569.

³ Gilbert et Claude. *Arch. gén. de méd.*, Paris, 1895, clxxv, 53.

⁴ Fagge, H. *Principles and Practice of Medicine*, 1886, ii, 280.



In 1925 Jeam collected 6 cases
of chronic jaundice due to this
cause.

explanation of *emotional jaundice*, but it has not received much support. It also explains jaundice in hysterical subjects when there is no evidence of any other causal factor. Jaundice in lead poisoning might, in the absence of any other satisfactory cause, be referred to spasm of the ducts. I have seen recurrent attacks of painful jaundice in a worker in lead, which did not appear to be due to gall-stones.

III. Jaundice due to Pressure exerted on the Bile-ducts from without.—*Synopsis*.—(1) By intrahepatic tumours. (2) By enlarged glands in the portal fissure: malignant, tuberculous, syphilitic; gumma in the portal fissure. (3) In lesions of the stomach: carcinoma, gastric ulcer, perigastric adhesions. (4) In duodenal lesions: ulcer, carcinoma. (5) By peritoneal adhesions. (6) By renal and suprarenal tumours: in nephroptosis. (7) Wandering spleen. (8) By retroperitoneal tumours. (9) In pancreatic lesions: carcinoma, cysts, chronic pancreatitis, gumma, calculus. (10) By aneurysm of the aorta, hepatic, mesenteric arteries. (11) In gastropptosis. (12) In hepatoptosis. (13) By uterine conditions and ovarian tumours. (14) Constipation.

(1) *Intrahepatic tumours*, such as carcinoma, may press on the intrahepatic branches of the bile-ducts, and if the obstructed area be large, such an amount of bile stasis may result as to lead to absorption of bile by the lymphatics and so to jaundice. In these cases bile may pass from the other lobe of the liver into the duodenum, so that the faeces retain their normal colour. A hydatid cyst or a gumma in the liver may act in a similar fashion. Primary or secondary malignant tumours of the liver may project into the portal fissure and press upon the hepatic ducts, the common hepatic or common bile-ducts, and so give rise to jaundice. A hydatid cyst or gumma, when projecting from the liver, may exert pressure on the bile-ducts in a similar manner.

In a case recorded by Legg¹ a hydatid cyst projecting from the liver compressed the common hepatic duct and caused persistent jaundice with xanthoma multiplex. Bristowe² described obstruction of both hepatic ducts by gummas.

(2) *Enlargement of the glands in the portal fissure* may be due to various causes, such as intrahepatic inflammation, malignant disease, and occasionally to tuberculosis, syphilis, and lymphadenoma. Malignant infiltration of the glands, which is the most frequent cause of jaundice, may be secondary to disease in the liver, gall-bladder, stomach, pancreas, intestine, or peritoneum.

Tuberculous glands in the portal fissure may in rare cases press on the bile-ducts and give rise to obstructive jaundice. Cases have been recorded by Florand,³ Köster,⁴ Knight,⁵ Hodenpyl,⁶ Lenoble and Attila.⁷

¹ Legg, J. W. *Trans. Path. Soc.*, Lond., 1874, xxv, 155.

² Bristowe, J. S. *Ibid.*, 1858, ix, 233.

³ Florand. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1899, 3. s., xvi, 30.

⁴ Köster. *Centralbl. f. inn. Med.*, 1896, xvii, 213.

⁵ Knight. *Quart. Med. Journ.*, Sheffield, 1895, iii, 372.

⁶ Hodenpyl. *Med. Rec.*, N.Y., 1898, liv, 693.

⁷ Lenoble et Attila. *Bull. Soc. Anat. Paris*, 1905, 6. s., vii, 781.

The rarity of tuberculous disease of the glands in the portal fissure depends on the fact that they receive the lymphatics from the liver, and not from the intestine and peritoneum. Tuberculous enteritis and peritonitis, therefore, infect the portal glands in a roundabout manner, viz. by producing tuberculosis of the portal spaces in the liver—the bacilli travelling by the portal vein. The lymphatics of the liver then convey the infection to the portal glands. It is conceivable that tuberculous infection might extend along the lymphatic trunks against the flow of lymph and so spread to the portal fissure from the abdominal cavity. Tuberculous enlargement of the portal glands is, therefore, closely bound up with tuberculosis of the liver (*vide* p. 336), in which, however, jaundice is most exceptional. A tuberculous gland in the portal fissure has been known to open into the common bile-duct (Köster), much in the same way that tuberculous bronchial glands have been found to open into the bronchi. Tuberculous glands may become adherent to the structures in the portal fissure and render any attempt at removal both difficult and dangerous. In Florand's case removal of tuberculous glands compressing the common bile-duct was followed by fatal hæmorrhage from the portal vein. Tuberculous retroperitoneal lymphatic glands may compress the common bile-duct near its entrance into the duodenum and give rise to obstructive jaundice. The glands may so indent the pancreas as to look at first like tuberculosis of that organ.

Syphilitic Adenitis.—It has been suggested that enlargement of the glands in the portal fissure may cause the specific jaundice sometimes seen in secondary syphilis, but this is doubtful (*vide* p. 350). It is possible that gummatous change or syphilitic adenitis later in the course of the disease may involve lymphatic glands in the neighbourhood of the bile-ducts, and, by pressure, cause obstructive jaundice. This condition is closely allied to gummatous infiltration about the head of the pancreas (*vide* p. 560).

A man aged thirty-two years under my care with chronic jaundice was explored by Mr. A. M. Sheild, and some hard masses were felt along the course of the common bile-duct. Although there was no manifest evidence of syphilis, he was put on iodides and mercury and became completely cured. The absence of any roseola, or, indeed, of any history of syphilis, made it unlikely that this case was one of jaundice in the early stages of syphilis (*vide* p. 349), and it may have been due to gummatous adenitis.

A *gumma in the portal fissure* may press on or involve the bile-ducts and so give rise to jaundice.

S. West¹ described a large gumma extending from the diaphragm to the neck of the gall-bladder, measuring $4\frac{1}{2} \times 2\frac{1}{2}$ inches. The patient, a girl aged fifteen years with jaundice, was the subject of congenital syphilis. Cases of delayed hereditary syphilis with jaundice due to constriction of the bile-ducts by dense adhesions have been recorded by Mackenzie² and Lazarus-Barlow.³

¹ West, S. *Trans. Path. Soc.*, Lond., 1890, xli, 155.

² Mackenzie, H. W. G. *Ibid.*, 1892, xliii, 84.

³ Lazarus-Barlow, W. S. *Ibid.*, 1899, l, 158.



(3) *Lesions of the Stomach.*—Jaundice occurs in from 4 to 13 per cent of all cases of *gastric carcinoma*. It occurs more often in cases in which the lesser curvature and the pylorus are affected, and is less frequent when the cardiac end of the stomach is involved.

Jaundice was present in 4 per cent of Osler and McCrae's¹ cases, in 5.5 per cent of Brinton's² cases, and in 13.7 per cent of Fenwick's.³

Usually jaundice is due to pressure exerted by enlarged lymphatic glands on the ducts, either in the portal fissure or close to the head of the pancreas. In some cases of carcinoma of the pylorus or of the lesser curvature of the stomach the growth spreads by continuity into the lesser omentum and may thus surround the common bile-duct and compress and invade its walls (compare case on p. 510).

This was well shewn in a case of spheroidal-celled carcinoma of the pylorus in a boy aged sixteen years who died in St. George's Hospital with jaundice.

In secondary malignant disease of the liver jaundice is more frequent when the primary growth is in the stomach than when it is in some more distant part of the abdomen, such as the rectum. The explanation of this is that jaundice is less often due to the actual metastases in the liver itself than to glandular infection in the immediate neighbourhood of the ducts or to the direct spread of growth into the lesser omentum.

In Gastric Ulcer and Perigastritis.—Jaundice due to the spread of inflammatory adhesions from a gastric ulcer near the pylorus must be very rare, as it is not mentioned by Murchison, Brinton, or by Dreschfeld.⁴ That it may occur is shewn by the following case.⁵

A man aged twenty-seven came under my care in St. George's Hospital with ~~no definite history whatever of gastric ulcer, but with dyspepsia and occasional vomiting of six weeks' duration and jaundice of two weeks' standing.~~ The stomach was dilated and a definite pyloric tumour with what was thought to be thickening of the adjacent curvatures was palpable. The case was regarded as carcinoma of the pylorus, but as unsuitable for gastro-enterostomy. At the necropsy there was no malignant disease, but a cicatrising ulcer at the pylorus giving rise to marked narrowing of that orifice and extensive peripyloric adhesions involving the common duct. The head of the pancreas, which was enlarged from chronic interstitial pancreatitis, had been felt in life and regarded as thickening of the curvatures of the stomach near the pylorus.

A case of jaundice and ascites in a man aged thirty-nine years due to fibrosis spreading from an ulcer near the pylorus to the portal fissure is recorded by James.⁶ The common bile-duct was normal, but the two hepatic ducts were compressed by cicatricial tissue which spread into the liver along the portal spaces.

¹ Osler and McCrae. *Cancer of the Stomach*, p. 55, 1900.

² Brinton. *Diseases of the Stomach*, p. 212, 1864.

³ Fenwick, S. *Cancer and Tumours of the Stomach*, p. 69, 1902.

⁴ Dreschfeld, J. *Allbutt's System of Medicine*, 1907, iii, 442.

⁵ Rolleston. *Practitioner*, Lond., 1897, lix, 465.

⁶ James. *Scot. Med. and Surg. Journ.*, 1898, ii, 511.

The converse condition of pyloric obstruction due to pericholecystitic adhesions is much less rare (*vide* p. 758).

(4) *Duodenal Lesions*.—In very rare instances *duodenal ulcer* is associated with jaundice ~~either~~ (i) as a complication or (ii) as an after-result.

(i) Ulceration ~~of the duodenum~~ is almost always confined to the first part of the duodenum and hardly ever extends sufficiently far into the second part to invade the biliary papilla. Concomitant duodenal catarrh, however, may spread to the biliary papilla. ~~Perry and Shaw~~¹ record several cases of duodenal ulcer with jaundice.

(ii) If, as rarely happens, the ulcer is in the second portion of the duodenum and involves the papilla, cicatricial contraction may cause permanent obstructive jaundice; Moynihan² has collected 11 cases of this sequel.

Inflammatory adhesions may spread out from a duodenal ulcer in the first part and compress the common bile-duct as it runs towards the biliary papilla. This mechanism is exactly like that already described in peripyloric adhesions. Moynihan refers to 5 such cases.

Carcinoma of the duodenum is not common, and need not interfere with the outflow of bile unless the growth is in the second part of the duodenum and involves the biliary papilla by extension or starts in the intestinal mucous membrane of the biliary papilla. This latter form of duodenal carcinoma—juxta-ampullary or perivaterian—imitates carcinoma of the head of the pancreas by presenting deep jaundice and distension of the gall-bladder (*vide* p. 557), but ~~in addition~~ it has a special tendency to set up infective cholangitis, multiple foci of suppuration in the liver, and fever. Specimens of this condition are to be found in the museums of St. Bartholomew's, Guy's, St. George's, and St. Thomas's Hospitals. The following case illustrates this sequence.

Carcinoma of Biliary Papilla, Jaundice, Suppurative Cholangitis, Secondary Abscesses in Prostate and Kidneys.—A man aged fifty-two years was in St. George's Hospital with jaundice of ten months' duration, which, however, had disappeared for one month during this period of ten months, loss of strength and flesh, and difficulty in passing water. The liver was much enlarged, but not tender; there was no ascites. The urine contained bile, pus, and indican. He had a greatly enlarged prostate, some diarrhoea, and a hectic temperature during the last five weeks of life. The diagnosis was malignant disease of the prostate with a secondary growth in the portal fissure producing jaundice. The necropsy shewed a carcinomatous growth involving the duodenal surface of the biliary papilla, with great dilatation of the common and of all the bile-ducts in the liver, universal suppurative cholangitis, and empyema of the gall-bladder. The liver was green, not fibrosed, and contained secondary nodules of white growth. The pancreatic duct was dilated. The enlargement of the prostate was due to an abscess; there were numerous abscesses in the kidneys.

¹ Perry and Shaw. *Guy's Hosp. Rep.*, 1893, 1, 273.

² Moynihan. *Duodenal Ulcer*, p. 223, 1910.

as (1) the only manifestation - the icteric form of duodenal ulcer (Bickel) which may irritate catarrhal jaundice, and may be due to poisons absorbed from the ulcers acting on the liver cells and causing hepatic insufficiency, or to an ascending cholangitis, or to cicatrization.

Zooßfel argues that swelling of the duodenal mucosa alone may obstruct the exit of bile

Cicatrization following a perforated duodenal ulcer may constrict the common bile duct (Sneath).

1 The duodenal contents may contain blood and be devoid of both bile and pancreatic ferments, and so differ from pancreatic and bile duct carcinoma; at a late stage

Bickel, G. Arch. des mal. de l'appar. digest., Paris, 1923, xiii, 833

Zooßfel. Klin. Wchnchr., 1923, ii, i. 422

Sneath, W A Brit. Med. Journ., 1918, i, 531.



Cases of perivaterian carcinoma of the duodenum without marked jaundice have been recorded by Lannois and Courmont,¹ Mauclaire and Durrieux,² and by Descos and Bériel.³

Carcinoma of the duodenum may cause jaundice in another way, viz. by inducing gastropsis, which, if there are adhesions around the ducts, may induce kinking and jaundice (*vide* p. 561).

Mackie Whyte⁴ recorded a case in which cancer of the duodenum, not involving the biliary papilla, led to great distension of the stomach and so to kinking of the common bile-duct and jaundice.

(5) *Peritoneal adhesions* around the hepatic or common bile-ducts may produce kinking of the ducts and thus lead to jaundice. Such adhesions may be due to local peritonitis set up in various ways, such as by gall-stones in the gall-bladder, perigastric inflammation (p. 553), adhesions around a duodenal ulcer (p. 554), adhesions to inflamed retroperitoneal glands (B. Robinson⁵), tuberculous peritonitis⁶ (Dujon,⁶ Berthomier⁷), or possibly by adhesions due to perihepatitis (S. Phillips⁸). It is, however, remarkable how seldom perihepatitis and chronic peritonitis are accompanied by jaundice.

(6) *New growths of the right kidney or suprarenal* very seldom press on the bile-duct and so directly produce jaundice, but secondary growths in the portal fissure may set up jaundice.

In 26 cases of primary malignant disease of the suprarenal bodies jaundice was not present in any (Rolleston and Marks⁹). A *tuberculous right kidney* has been known to compress the common bile-duct and cause jaundice (Tixier¹⁰).

That a *floating kidney* can exert direct pressure on the bile-ducts and thus lead to jaundice, as suggested by Litten,¹¹ is regarded as improbable by Macalister.¹² The colic, jaundice, and vomiting induced by a floating kidney on the right side may be explained in the following way: the peritoneum over the kidney being continuous with that covering the duodenum and common bile-duct, undue mobility of the kidney will exert traction on the duodenum and common bile-duct and will lead to narrowing of the bile-duct and duodenum. Nephroptosis may also lead to downward displacement of the duodenum, with stretching of the common bile-duct, displacement of the gall-bladder, with sharp kinking of the cystic duct, torsion of the vertical part of the duodenum, and

¹ Lannois et Courmont. *Rev. de méd.*, Paris, 1894, xiv, 291.

² Mauclaire et Durrieux. *Bull. Soc. Anat. Paris*, 1897, lxxii, 721.

³ Descos et Bériel. *Rev. de méd.*, Paris, 1899, xix, 633.

⁴ Whyte, M. *Scot. Med. and Surg. Journ.*, 1897, i, 361.

⁵ Byron Robinson. *Am. Med.-Surg. Bull.*, N.Y., 1896, ix, 518.

⁶ Dujon. *Procès-verbaux, XIX. Congrès de chir.*, 1906, p. 166.

⁷ Berthomier. *Rev. de chir.*, Paris, 1910, xlii, 1179; MOUÏSSET et GALE. *Lyon méd.*, 1913, cxx, 433.

⁸ Phillips, S. *Lancet*, Lond., 1903, i, 1796.

⁹ Rolleston and Marks. *Amer. Journ. Med. Sc.*, Phila., 1898, cxvi, 398.

¹⁰ Tixier. *Rev. de chir.*, Paris, 1910, xli, 443.

¹¹ Litten. *Charité-Ann.*, Berlin, 1880, v, 10.

¹² Macalister, A. *Allbutt's System of Medicine*, 1897, iv, 346.

perhaps even of the bile-duct (J. Hutchinson, Jr.¹). A floating kidney may not only cause colic and jaundice, but the displaced kidney may readily be mistaken for a distended gall-bladder (Hutchinson). Cases of jaundice diagnosed as cholelithiasis and proved to be due to floating kidneys have been recorded by MacLagan and Treves² (3), Hale White,³ Cordier,⁴ Fenwick,⁵ Lawrie,⁶ Marwedel,⁷ Sherren.⁸

The diagnosis depends on the detection of a floating kidney, for the symptoms, biliary colic and jaundice, are the same as those of cholelithiasis. The attacks of pain are rare at night in floating kidney, common in cholelithiasis (Sherren). If the symptoms persist after the floating kidney has been efficiently and successfully treated, it is probable that there is cholelithiasis in addition.

(7) *Wandering Spleen*.—The traction exerted through the pancreas on the common bile-duct by the elongated pedicle of a wandering spleen has been thought to account for jaundice when it occurs, which is but rarely, in this condition (Bland-Sutton⁹).

(8) *Retroperitoneal tumours* in rare instances press on the common bile-ducts and cause jaundice.

Vander Veer¹⁰ recorded a large retroperitoneal myxosarcoma (weight 6 pounds) arising from the region of the left adrenal, which so interfered with the bile-duct as to produce jaundice. In a male child, aged two and a half years, under my care, with a round-celled retroperitoneal sarcoma near the right suprarenal and numerous secondary growths in the neighbouring lymphatic glands, jaundice, which was not absolutely obstructive, since the faeces were not devoid of pigment, was present for eight weeks before death.

A hydatid cyst arising in the retroperitoneal space near the head of the pancreas may compress the common duct. This is illustrated by a specimen (No. 2256) in St. Bartholomew's Hospital Museum.

(9) *Lesions of the Pancreas*.—Malignant tumours, cysts, chronic interstitial inflammation, gumma, and calculi in Wirsung's duct may all compress the common bile-duct and produce obstructive jaundice, but with the exception of the first named are rarely recognised as acting in this manner.

Malignant tumours of the pancreas may be primary or secondary, but it is almost entirely with primary malignant disease that we are at present concerned. It is practically always carcinoma, and usually attacks the head of the gland—according to Hale White,¹¹ in 85 per cent of the cases.

¹ Hutchinson, J., Jr. *Practitioner*, 1902, lxxviii, 186.

² MacLagan and Treves. *Lancet*, Lond., 1900, i, 15.

³ Hale White. *Brit. Med. Journ.*, 1892, i, 223.

⁴ Cordier. *Amer. Journ. Obst.*, 1898, xxxiv, 532.

⁵ Fenwick. *Lancet*, Lond., 1899, ii, 1296.

⁶ Lawrie. *Brit. Med. Journ.*, 1901, i, 15.

⁷ Marwedel. *Beitr. z. klin. Chir.*, 1902, xxxiv, 478.

⁸ Sherren. *Lancet*, Lond., 1911, i, 870.

⁹ Bland-Sutton. *Gallstones and Diseases of the Bile-ducts*, p. 146, 1907.

¹⁰ Vander Veer. *Amer. Journ. Med. Sc.*, Phila., 1892, ciii, 22.

¹¹ Hale White. *Guy's Hosp. Rep.*, 1900, liv, 17.



The ~~simplest~~ examination of the
duodenal contents showing absence
of pancreatic ferments as well
as of bile may assist in the
diagnosis

When in this situation, the growth readily compresses the common bile-duct near its termination, but when the growth is limited to the tail or body of the pancreas, jaundice does not result unless a secondary growth compresses the duct or there is some other cause for jaundice, such as a calculus in the common duct. Jaundice occurs in a majority of cases of primary malignant disease of the pancreas.

Mirallié¹ found it in 82 out of 113 cases. Oser gives two-thirds as the proportion of cases in which jaundice occurs. The occurrence or absence of jaundice mainly depends on the anatomical relation of the head of the pancreas to the common bile-duct (*vide* p. 559).

The jaundice may come on gradually and painlessly, or be accompanied by colic. It is permanent and progressive, and becomes intense, so that cholaemia develops comparatively early. The other distinctive features of malignant disease of the head of the pancreas are rapid and extensive wasting, a tumour in the position of the pancreas, which, however, is seldom palpable, and a distended gall-bladder. The association of deep jaundice with a large gall-bladder is sometimes spoken of as the sign of Bard and Pic.² It illustrates Courvoisier's law that biliary obstruction due to new growth is accompanied by an enlarged gall-bladder, whereas in gall-stone obstruction of the common duct the gall-bladder is small. As a matter of fact, however, the gall-bladder, even though enlarged as shewn by necropsy, is not always palpable during life. ~~It is practically impossible to distinguish it from primary carcinoma of the common bile-duct, except by means of Cammidge's tests ; this point is discussed on p. 699.~~ In primary carcinoma of the ampulla of Vater (*vide* p. 702) and of the duodenal surface of the biliary papilla the jaundice may intermit, which it never does in malignant disease of the pancreas, and fever from infective cholangitis may supervene. From a calculus in the common duct the diagnosis may be easy when the cases are typical, but sometimes it is difficult, as attacks of pseudo-biliary colic may occur about the time of the onset of jaundice in malignant disease of the pancreas, and pain may be absent in some cases of calculus in the common duct. The history of the cases and the course of the disease, especially the character of the jaundice, progressive or intermittent, and the condition of general nutrition will usually clear up a diagnosis which at first was doubtful.

Cammidge's Tests.—By treating the urine, free from sugar, of cases of pancreatitis by a special method, which cannot be described further here except to state that the urine is first boiled with HCl and then with sodium acetate and phenyl-hydrazine hydrochloride, Cammidge³ obtained crystals which could

¹ Mirallié. *Gaz. des hôp. de Paris*, 1893, lxvi, 889.

² Bard et Pic. *Rev. de méd.*, Paris, 1888, viii, 257.

³ Cammidge. "The Chemistry of the Urine in Diseases of the Pancreas," *Lancet*, Lond., 1904, i, 783; "An Improved Method of performing the 'Pancreatic Reaction' in the Urine," *Brit. Med. Journ.*, 1906, i, 1150; "Urine in Chronic Disease of the Pancreas," *Proc. Roy. Soc.*, Lond., 1909, Ser. B, pp. 81-372; *Proc. Roy. Soc. Med.*, Lond., 1910, iii (Med. Sect.), 163.

not be got from normal urine. The crystals are due to a pentose derived from the pancreatic nucleo-protein which passes into the blood as a result of degeneration of the gland cells. Jaundice due to pancreatitis can thus be distinguished from jaundice due to other causes, and malignant disease of the pancreas, in which "pancreatic reaction C" is not obtained, can be diagnosed from inflammatory affections of the pancreas. From examination of the faeces Cammidge also obtains results important in diagnosis: an acid reaction is in favour of pancreatic disease, for in gall-stone obstruction of the ducts the reaction is usually alkaline. The percentage of unabsorbed fat is higher in carcinoma of the pancreas than in growths of the ducts. The unsaponified fats are in excess of the saponified in diseases of the pancreas, whereas the reverse holds good in obstruction of the common duct by stone or growth when the pancreas is unaffected. These conclusions have been freely criticised.

Carcinoma of the pancreas may be associated with cholelithiasis, and in rare instances with gall-stones in the common duct.

A woman aged fifty-eight, under my care in St. George's Hospital, was thought to be suffering from gall-stone obstruction and was accordingly operated upon; a gall-stone was felt, and on manipulation was displaced, it was thought, into the duodenum. Death occurred on the third day, largely from haemorrhage at the site of operation. At the necropsy it was found that the calculus had been pushed back into the gall-bladder, and that all the ducts were greatly dilated. The gall-bladder was small and contained two round large calculi. The head of the pancreas contained a colloid carcinoma which did not involve the duct, so the jaundice was probably due to the stone in the common duct. Microscopically the growth was a colloid spheroidal-celled carcinoma.

Pancreatic cysts rarely press on the bile-ducts and cause jaundice. Pancreatic and peripancreatic cysts may present in various situations: (i) Above the stomach and below the liver (interhepato-gastric type). (ii) Between the greater curvature of the stomach and the transverse colon; this is the commonest form (subhepato-gastric type). (iii) Below the transverse colon, so that the cyst projects near the umbilicus (subhepato-gastro-colic type). Cysts which pass forwards between the stomach and the transverse colon (subhepato-gastric type) may compress the common bile-duct. Oser¹ collected 15 cases in which jaundice occurred.

A man aged thirty, with jaundice of three months' duration, under my care in St. George's Hospital, was operated upon by Mr. G. R. Turner, and a pancreatic cyst found projecting between the greater curvature of the stomach and the transverse colon.² After drainage the jaundice disappeared and the man recovered. Turney and Ballance³ met with a case of jaundice in a man aged thirty-five in whom the symptoms were ascribed to calculous obstruction of the common bile-duct; laparotomy, however, proved that the jaundice was

¹ Oser. *Nothnagel's Encyclopedia of Practical Medicine*, p. 195, English Transl., 1903.

² *Vide also Trans. Med. Soc. Lond.*, 1898, xxi, 94.

³ Turney and Ballance. *St. Thomas's Hosp. Rep.*, 1898, xxvi, 119.



It has been suggested that
Jaundice in mumps may be
caused by metastatic
pancreatitis (Batten)

to infection of the biliary
tract, and to syphilis
(Mallet-Guy). The gall
bladder may or may not
be distended,

Batten. Quoted by Gallies. Proc. Royal Soc.
Med. 1911.

Mallet-Guy, Pancreatites chroniques avec ictere.
Paris, 1925 p 69.

due to the pressure of a pancreatic cyst. Cases have also been described by de Havilland Hall,¹ McPhedran.²

A hydatid cyst in the pancreas is a pathological curiosity.

A hydatid cyst in the head of the pancreas caused jaundice of ten months' duration and ascites in a boy aged six years. At the necropsy the gall-bladder was dilated and the bile-duct and portal vein were stretched over the cyst and so compressed that it was impossible to force bile from the distended gall-bladder into the duodenum before the cyst was opened. The liver was enlarged, granular on the surface, and fibrosed.³

Acute Pancreatitis.—It has been suggested by Oser and Mayo Robson⁴ that the condition ordinarily called catarrhal jaundice is the result of catarrhal inflammation of the head of the pancreas which presses on the common duct (*vide* p. 664). A Jaundice is very rare in the graver forms of acute pancreatitis; but haemorrhagic pancreatitis may be associated with jaundice when there is a small stone in the orifice of the biliary papilla (*vide* p. 750).

Chronic Interstitial Pancreatitis.—Mayo Robson⁵ and Barling⁶ pointed out that chronic inflammation of the head of the pancreas may compress the common bile-duct and produce a train of symptoms—obstructive jaundice, colic, and wasting—strongly suggesting malignant disease or impacted gall-stones. Whether chronic pancreatitis will or will not compress the common bile-duct depends on the anatomical relation of the common bile-duct to the head of the pancreas. In 38 per cent of bodies the duct passes behind the head of the pancreas, and in these cases chronic pancreatitis need not affect the common bile-duct. In 62 per cent of bodies the common bile-duct is embedded in the head of the pancreas (Helley⁷), and in these cases chronic pancreatitis would compress the common duct and cause jaundice. In 62 per cent of cases of chronic pancreatitis associated with gall-stones bile-pigment was present in the urine (Robson and Cammidge⁸). This chronic fibrosis may be directly due to gall-stones in the common duct and may persist after the stone is expelled. The diagnosis is difficult, and the moral is that it is advisable to admit such cases to operation. In some instances the gall-bladder has been drained, either externally or into the small intestine, and in other cases the abdomen has been closed without any more radical measure than manipulation of the parts. Recovery has followed these surgical procedures. It is possible that when the parts have merely been

¹ de Havilland Hall. *Trans. Med. Soc. Lond.*, 1898, xxi, 107.

² McPhedran. *Trans. Assoc. Am. Phys.*, 1897, xii, 61.

³ Guy's Hospital Museum, No. 1475.


⁴ Robson, Mayo. *Lancet*, Lond., 1904, i, 770.

⁵ *Idem.* *Ibid.*, 1900, ii, 236.

⁶ Barling. *Brit. Med. Journ.*, 1900, ii, 1766.

⁷ Helley. *Arch. f. mikr. Anat.*, Bonn, 1898, lii, 773.

⁸ Robson and Cammidge. *The Pancreas, its Surgery and Pathology*, p. 319 (W. B. Saunders Co., 1907).

manipulated (Owen,¹ Dalziel²) a calculus in the orifice of the biliary papilla has been displaced into the duodenum. It seems highly probable that cases of chronic interstitial pancreatitis have been regarded not only during life, but even after death, as examples of carcinoma of the head of the pancreas. According to Hale White,³ ~~however,~~ chronic interstitial pancreatitis is rare; for among 20,000 necropsies at Guy's Hospital only 4 cases ~~of this disease~~ were recognised. ~~This conclusion as to its rarity is open to justifiable criticism.~~ 

In cases of pancreatitis the secretion of the gland escapes into the surrounding tissues and sets up fat necrosis. As a result of this glycerin and fatty acids are liberated. It was first thought that the tendency to hæmorrhage, both in acute and chronic pancreatitis, which is so often accompanied by chronic jaundice, might be due to the action of glycerin (Mayo Robson⁴), but subsequently Mayo Robson⁵ referred it to a diminution of the lime salts in the blood depending on increased excretion of oxalates in the urine.

Closely allied to chronic interstitial pancreatitis is the extremely rare condition gummatous infiltration in and around the head of the pancreas.

Gumma.—In a man aged thirty-three who had had syphilis ten years previously, and was suffering from obstructive jaundice, H. B. Robinson⁶ opened the abdomen, felt a growth in the situation of the head of the pancreas, and accordingly put the gall-bladder into communication with the hepatic flexure of the colon. Under iodide of potassium the mass disappeared and there was a gain in weight of two stone. A similar case of Da Costa's is mentioned in Gould's *Year-Book of Surgery* for 1902, p. 181. Moynihan⁷ has also described this condition.

A large pancreatic calculus in the ampulla of Vater, or in the termination of Wirsung's duct, so that it compresses the end of the common bile-duct, may give rise to jaundice (Pearce Gould,⁸ Kinnicutt,⁹ Murray¹⁰).

(10) *Aneurysms of the abdominal aorta* near the coeliac axis may press on the common bile-duct and so cause jaundice and dilatation of the gall-bladder.

In a man aged twenty-eight, who had syphilis when twenty years of age, a sacculated aneurysm involving the origin of the coeliac axis burst into the second part of the duodenum a short distance above the biliary papilla. The common bile-duct was compressed and the gall-bladder distended. Jaundice occurred three days before death, which was preceded by sudden and profuse hæmatemesis (W. L. Dickinson¹¹). Stokes¹² previously reported a case.

¹ Owen, *Brit. Med. Journ.*, 1902, ii, 1311; and Hale White, *ibid.*, 1903, ii, 126.

² Dalziel. *Ibid.*, 1902, ii, 1312.

³ Hale White. *Clin. Journ.*, Lond., 1907, xxx, 278.

⁴ Robson, Mayo. *Brit. Med. Journ.*, 1901, i, 1131.

⁵ *Idem.* *Lancet*, Lond., 1904, i, 770.

⁶ Robinson, H. B. *Brit. Med. Journ.*, 1900, ii, 1004.

⁷ Moynihan. *Lancet*, Lond., 1902, ii, 856.

⁸ Gould, A. P. *Trans. Clin. Soc.*, Lond., 1899, xxxii, 59.

⁹ Kinnicutt. *Amer. Journ. Med. Sc.*, Phila., 1902, cxxiv, 948.

¹⁰ Murray. *Lancet*, Lond., 1912, i, 793.

¹¹ Dickinson, W. L. *Trans. Path. Soc.*, Lond., 1891, xlii, 77.

¹² Stokes. *Diseases of the Heart and Aorta*, p. 633, 1854.

^ | fatal

Bosanquet, however, from microscopic examination estimates that it occurs in 5 per cent of all necropsies

Bosanquet. Lancet, Lond., 1905, 1, 977

Aneurysm of the hepatic artery may compress the bile-ducts above the entrance of the cystic duct, and hence the gall-bladder need not be dilated, as in jaundice due to an aortic aneurysm. Jaundice occurred in 16 out of 41 cases (Rolland¹).

An *aneurysm of the superior mesenteric artery* near its origin from the aorta has been known to compress the bile-duct and give rise to jaundice (J. A. Wilson,² W. T. Gairdner³). The majority of aneurysms on this vessel, however, are not associated with jaundice. Those on the peripheral portions of the artery are not in relation with the bile-ducts, and therefore do not compress them.

(11) *Gastroptosis* is not infrequent, but is rarely associated with jaundice. Steele⁴ states that gastroptosis alone cannot exert sufficient pressure on the bile-ducts to obstruct the flow of bile; this is based on his observations that after death downward displacement of the pylorus, so as to imitate the conditions present in gastroptosis, though it stretched the gastrohepatic omentum, did not interfere with the passage of bile into the duodenum: If, however, there were any adhesions involving the ducts in the portal fissure, very moderate displacement of the pylorus produced kinking of the ducts and obstruction. It would thus appear that in the presence of adhesions around the ducts, gastroptosis will readily produce jaundice.

(12) *Hepatoptosis*.—In wandering liver jaundice may be due to the presence of gall-stones, to concomitant catarrh of the ducts, to a floating right kidney, or to twisting of the common bile-duct. Dutton Steele⁵ collected 15 cases of hepatoptosis in which there were attacks of jaundice without gall-stones. In Crawford's⁶ case of anteverted liver the bile-duct had apparently been twisted, so as to cause jaundice, at the junction of the common bile and cystic ducts. The descent or dropping of the liver tends to produce this twisting. By injection experiments on the dead body Dutton Steele shewed that the more the liver descends towards the pelvis, the more difficult it is to drive injection from the biliary papilla into the gall-bladder.

(13) *Uterine Conditions, Ovarian Tumours*.—The pressure of a pregnant uterus on the ducts has been regarded as responsible for jaundice (Murchison⁷). This is very doubtful; mild jaundice in pregnant women is usually due to gastro-duodenal catarrh, but may be due to gall-stones, cholangitis, or toxæmic inflammation of the small intrahepatic ducts. The occurrence of acute yellow atrophy is especially favoured by pregnancy (*vide* p. 576).

Ovarian tumours may exceptionally cause jaundice by pressure on the bile-ducts (Poynder⁸). On the other hand, jaundice may be merely

¹ Rolland. *Glasgow Med. Journ.*, 1908, lxi, 342.

² Wilson, J. A. *Med.-Chir. Trans.*, Lond., 1841, xxiv, 221.

³ Gairdner, W. T. *Clinical Medicine*, p. 504, 1862.

⁴ Dutton Steele. *Univ. Med. Mag.*, Phila., 1901, xiii, 838.

⁵ Idem. *Univ. Penn. Med. Bull.*, Phila., 1903, xv, 424.

⁶ Crawford, R. P. *Lancet*, Lond., 1897, ii, 1182.

⁷ Murchison. *Lectures on Diseases of the Liver*, p. 358, 2nd ed., 1877.

⁸ Poynder. *Ind. Med. Gaz.*, 1899, xxxiv, 208.

associated with ovarian cysts and depend on catarrhal inflammation of the papilla, infective cholangitis, or gall-stones. The abdominal distension caused by an ovarian cyst favours stagnation of bile, infection of the ducts, and cholelithiasis. Thus suppurative cholangitis or cholecystitis may complicate ovarian cysts.

(14) *Constipation* may be associated with jaundice. Slight jaundice may possibly be due to absorption of poisons from the intestine producing catarrh of the intrahepatic bile-ducts, or in other cases be due to the spread of associated duodenal catarrh to the common duct. In this way the relief of jaundice after free purgation may be explained. It is improbable that faecal accumulation by direct pressure can give rise to jaundice. But in rare cases in which the colon is firmly united to the under surface of the liver by adhesions, faecal accumulation in the transverse colon may possibly lead to kinking or compression of the common bile-duct.

General Remarks on the Diagnosis of Jaundice.—The large number of conditions which may give rise to jaundice makes it essential that a careful examination should be made for any other evidence of disease. Thus the existence of a tumour in the abdomen, breast, or rectum will suggest malignant disease, and the presence of syphilis, either in the secondary or tertiary stage, should be an indication for specific treatment. The following points have a bearing on the nature of jaundice in a given patient.

Age.—Slight and transient jaundice appearing within a few days of birth is benign or physiological, but if well marked and accompanied by constitutional symptoms and fever, should suggest a grave form of jaundice due either to severe infection of the umbilical cord or to some haemic infection (*vide p. 571*). Persistent jaundice from birth is in favour of congenital obstruction in the larger bile-ducts (*vide p. 649*), which is usually rapidly fatal; in rare instances jaundice may persist from birth into adult life (*vide p. 573*). In childhood and early adult life catarrhal jaundice is common. Between the ages of thirty and forty-five years gall-stones, especially in women, are the most probable cause; later in life malignant disease and cirrhosis must be taken into account.

Sex.—Women are more prone to gall-stones and to malignant disease; men to cirrhosis and perhaps to the infectious forms of jaundice, such as Weil's disease. Pregnant women seem more susceptible than others to acute yellow atrophy. In very rare instances jaundice recurring during pregnancy only has been noted. Benedict¹ reported this in two sisters; in my case three infants of a woman thus affected died with jaundice.²

Familial Jaundice.—The occurrence of jaundice in several members of the same family may be due to some acute infection, as in Weil's disease, and is seen in epidemic jaundice. Chronic jaundice in members of the same family is met with in chronic splenomegalic haemolytic jaundice and occasionally in hypertrophic biliary cirrhosis.

¹ Benedict. *Deutsche med. Wchnschr.*, 1902, xxviii, 296.

² Rolleston. *Brit. Med. Journ.*, 1910, i, 864.

I have seen distension of ascending colon cause
jaundice which immediately passed off when the
distension was relieved, but recurred with
a return of the colic distension

Onset.—If preceded by gastro-intestinal disturbance, catarrhal jaundice should be thought of; if by severe colic, gall-stones. A gradual onset with no special or striking symptoms should suggest the pressure of a tumour on the ducts. Repeated and transient attacks are in favour of gall-stones. Epidemic jaundice suggests some form of infective jaundice, such as Weil's disease.

Pain.—Constant pain suggests malignant disease; intermittent attacks point to gall-stones. Biliary colic may also occur when hydatid membranes are passed through the ducts and occasionally when malignant disease involves the ducts—pseudo-gall-stone colic. Absence of pain, however, does not exclude malignant disease, though it is the rule in catarrhal jaundice and in cirrhosis.

Duration and Progress.—Jaundice of short duration is most commonly catarrhal or due to gall-stones. If continued for more than six months, malignant disease is unlikely, and biliary cirrhosis or impacted gall-stone should be thought of. Jaundice lasting for years is probably due to haemolytic jaundice or to biliary cirrhosis.

Progressive and black jaundice suggests malignant disease, while chronic jaundice which varies from time to time is more compatible with a stone impacted in the common duct or biliary cirrhosis.

Degree and Intensity of Jaundice.—Slight icterus may be catarrhal, or, if associated with fever and constitutional disturbance, toxæmic. Persistent slight jaundice with splenomegaly suggests chronic haemolytic jaundice. The commonest causes of deep jaundice are malignant disease, impaction of a gall-stone in the common duct, and biliary cirrhosis. Extremely deep jaundice almost postulates malignant disease; that accompanying gall-stone impaction is deeper than that of cirrhosis, but never equals that seen in compression of the common bile-duct by tumours, such as carcinoma of the head of the pancreas or malignant disease of the duct. ~~Jaundice which recurs is in favour of gall-~~
~~stones.~~

Outbreaks of jaundice in epidemics suggest some form of toxæmic or infectious jaundice.

Fever suggests toxæmic jaundice or, when associated with considerable splenic enlargement, biliary cirrhosis. Pyrexia, of course, occurs in calculous cholangitis, in hepatic suppuration, such as abscess or pylephlebitis, and occasionally in malignant disease.

The condition of the gall-bladder is of great importance in the diagnosis of the cause of jaundice. It is not enlarged or palpable in toxæmic or intrahepatic jaundice, in biliary cirrhosis, or when there is pressure on the hepatic ducts. Obstruction of the cystic duct usually leads to distension of the gall-bladder with mucus. In obstruction of the common bile-duct by tumours pressing on it from without, or arising in its walls, the gall-bladder is distended; on the other hand, in obstruction by gall-stones the gall-bladder, contrary to what might naturally be expected, is not enlarged. This is known as Courvoisier's law.

In 100 cases of obstruction of the common duct by causes other than calculi the gall-bladder was enlarged in 92, whereas out of 87 cases of calculous obstruction the gall-bladder was shrivelled up and small in 70, or 80 per cent (Courvoisier¹). Mayo Robson,² Tuffier,³ Tessier,⁴ and R. C. Cabot⁵ have supported Courvoisier's dictum. Cabot's figures are even more striking than Courvoisier's, and shew that the law is true in 95 per cent of the cases. The shrivelled condition of the gall-bladder in gall-stone obstruction of the common duct is partly the result of past cholecystitis and partly because the obstruction is usually not complete. It has also been suggested that in gall-stone obstruction the spiral valves of Heister in the cystic duct remain competent and prevent regurgitation from the common bile-duct, whereas in obstruction of the common duct by tumours these valves fail.

Condition of the Liver.—Great enlargement occurs in malignant disease, hypertrophie biliary cirrhosis, and in abscess. But in abscess jaundice is slight or absent. In malignant disease the surface is generally nodular and the enlargement is progressive; in hypertrophie biliary cirrhosis the liver is smooth and the spleen is much enlarged.

The association of *ascites* points to malignant disease or cirrhosis, but in cirrhosis jaundice is usually less marked than in malignant disease. Cutaneous haemorrhages in chronic jaundice point to pancreatic disease.

Examination of the *urine* and *faeces* helps to distinguish complete from partial obstructive and toxæmic jaundice. Cammidge's tests are of use in the diagnosis between jaundice due to pancreatitis, gall-stone obstruction, and malignant obstruction of the common bile-duct. Urobilinuria is in favour of inflammation of the ducts.

PROGNOSIS.—The occurrence of jaundice in certain diseases is of importance as shewing that hepatic complications have supervened; thus, when, as very rarely happens, jaundice is met with in typhoid fever, inflammation of the gall-bladder or ducts should be thought of. In puerperal eclampsia jaundice is of extremely bad omen; death usually follows in a few hours or days. The onset of jaundice after phosphorus poisoning is a sign that the liver is affected and must be regarded as of the gravest significance, since very few cases recover when this stage is reached. The onset of jaundice in a patient who has had malaria causes some anxiety at first, as it may be due to the severe hæmic infection of ~~haemoglobinuria~~ or "blackwater" fever. Jaundice in relapsing fever makes the prognosis grave (Sandwith⁶). Jaundice in the course of appendicitis makes the outlook bad, as septicaemia is the probable cause; according to Reichel⁷ 55 per cent of these cases die. λ

The ultimate prognosis in any given case of jaundice depends not so much on the degree of jaundice as on the underlying cause. Thus the comparatively slight icteric tint (toxæmic jaundice) in some cases of

¹ Courvoisier. *Path. u. Chir. d. Gallenwegen*, 1890.

² Mayo Robson. *Gall-stones and Their Treatment*, 1892.

³ Tuffier. *Semaine méd.*, Par., 1893, xiii, 55.

⁴ Tessier. *Ibid.*, 1893, xiii, 7.

⁵ Cabot, R. C. *St. Paul Med. Journ.*, Dec. 1901.

⁶ Sandwith. *Practitioner*, Lond., 1904, lxxii, 660.

⁷ Reichel. *Deutsche Ztschr. f. Chir.*, Leipz., 1907, lxxviii.

^ It has been stated that jaundice in pneumonia adds to the gravity of the prognosis (Lebert), but cholepneumonia followed by jaundice in the course of pneumonia is not necessarily a severe complication (vide Anders).

Lebert. quoted by Anders, American Med., 1905, ix, 431



pyaemia and the "black" jaundice of complete obstruction of the ducts in malignant disease do not differ very materially in their ultimate prognosis.

Prognosis in Chronic Jaundice.—When gall-stones in the common duct set up chronic jaundice there is a chance, though rather a slender one, that the calculus or calculi may pass and that a spontaneous cure may result. More commonly jaundice may disappear for a time as a result of bile escaping by the side of the gall-stone. Subsequently jaundice may return and may be accompanied by periodic attacks of pain, fever, and increase in jaundice or intermittent hepatic fever. In such cases the prognosis is good if operation for removal of the calculus is undertaken before the patient becomes weak or deeply jaundiced. But when continued fever has developed and there is reason to fear that suppurative cholangitis has supervened, the prognosis is very grave.

In hypertrophic biliary cirrhosis with chronic jaundice, though the chances of ultimate recovery are practically nil, life is often prolonged for years. In such cases the general state of nutrition and the length of the intervals between the exacerbations are points of importance in estimating the probable expectancy of life. Emaciation, weakness, and attacks repeated at short intervals point to death in the near future. When chronic jaundice is associated with splenic enlargement (chronic haemolytic jaundice, *vide* p. 537, and meta-icteric splenomegaly, *vide* p. 680) the prognosis is usually good. In fact, congenital chronic haemolytic jaundice appears to make little or no difference to the subject, for he can hardly be considered a patient.

In deep chronic jaundice, due to whatever cause, the prognosis is unfavourable, since if operation is undertaken, there is considerable danger from haemorrhage, even though large doses of calcium salts are given before the operation. While if the patient is not operated upon, cholaemia will develop sooner or later. In such cases good effects from iodide of potassium point to gummatous obstruction and make the prognosis good.

In chronic jaundice due to malignant disease the prognosis is necessarily fatal, but it is not quite so desperate in cases presumed to be malignant disease of the pancreas as in cases in which new growth is palpable elsewhere. The explanation of this statement is that some cases formerly regarded as slow-growing ("scirrhous") carcinoma of the head of the pancreas are in reality chronic interstitial pancreatitis (Mayo Robson¹).

In chronic jaundice much depends on the functional activity of the kidneys being well maintained; if the amount of urine falls and waste-products are less freely excreted, biliary toxæmia is likely to result. The presence of albuminuria points to the kidneys being damaged by the toxæmia accompanying the jaundice, and is, therefore, an index of a severe condition. The detection of leucine and tyrosine in the urine of a jaundiced patient makes the prognosis very grave.

When jaundice is accompanied by hepatic insufficiency, so that poisons which should have been destroyed by the liver escape into the general circulation and give rise to a general toxæmia, as shown by nervous

¹ Mayo Robson. *Lancet*, Lond., 1900, ii, 236.

symptoms, such as delirium, drowsiness, and coma, and by haemorrhages, the prognosis is very grave indeed, since life cannot be long maintained after the onset of cholaemia. Nervous symptoms in jaundice should always arouse anxiety. In some cases, at first quite indistinguishable from simple catarrhal jaundice, nervous symptoms somewhat rapidly appear, and then acute yellow atrophy of the liver supervenes. But in the recently described syndrome characterised by infective jaundice and meningeal symptoms¹ the prognosis is good. The condition which is acute may imitate cerebrospinal meningitis.

When chronic jaundice is accompanied by xanthoma, it may be assumed that the cause of the jaundice is not malignant disease, inasmuch as this would have killed the patient before this change would have had sufficient time to develop.

Treatment.—The radical and the only satisfactory course is the removal or cure of the underlying condition of which jaundice is a result; for this an accurate diagnosis in each case is essential. The methods of treatment in the various conditions giving rise to jaundice are dealt with elsewhere, and will not be repeated here. The necessity for a diagnosis of the cause in order to make successful treatment possible is shewn by the cure of jaundice in the early stage of syphilis by mercury, or when due to the pressure of a gumma on the ducts by iodides; or surgically by the removal of calculi from the common bile-duct in intermittent hepatic fever (p. 759).

Jaundice often depends on catarrhal inflammation of the ducts, which may be removed by medical measures which increase the flow of bile and so flush the bile-ducts, *e.g.* draughts of water containing salts in solution, drinking the waters at Harrogate, Neuenahr, Carlsbad, Vichy, and the administration of urotropin and salicylates. In some cases medical measures fail to remove catarrhal inflammation of the ducts and surgical interference in the form of free drainage may be necessary.

Symptomatic or Palliative Treatment.—Constipation should be prevented by exercises, plenty of water, salines, such as phosphate and sulphate of sodium, sulphate of magnesium, or the natural Carlsbad or other purgative waters, taken on an empty stomach before breakfast. The salts may be made more palatable by the addition of a little infusion of quassia or cinchona. If necessary, a few grains of calomel or of blue pill may be taken the night before. Vigorous purgatives should be avoided, as intestinal catarrh may be thus set up, or, if present, increased. For gastric catarrh careful dieting, bicarbonate of sodium, and for vomiting bismuth, dilute hydrocyanic acid, and warm applications to the abdomen should be ordered. For flatulence minute doses ($\frac{1}{10}$ grain) of calomel or of liquor hydrargyri perchloridi, guaiacol, naphthalene tetrachloride, salicylate of bismuth, creosote, turpentine in capsules, or salol may be given.

Fresh ox or pig's bile contained in capsules or keratin-coated pills,

¹ Guillian et Richet. *Bull. et mem. Soc. méd. des hôp. de Paris*, 1910, 3. s., xxviii, 289. Guillian. *Paris méd.*, 1912, No. 27, p. 9.

^ From experiments showing that ^{the blood-serum} ~~it~~ neutralizes the virus of acute poliomyelitis this condition appears to be due to that cause (Pignot).

Pignot. La Clinique, Par., 1913, viii, 734.

A meat diet is recommended
as preventing the depressing
effect left behind by Jaundice,
especially the Catarrhal form.
(Chevallier). Pig's liver has
been specially advocated

Chevallier. Prescribed, Paris, 1891, 470

so as to pass unaltered through the stomach, are sometimes given to replace the absent bile in the bowel, and may be taken three times a day before food.

For *pruritus*, which is often extremely troublesome and the cause of sleeplessness, several remedies may have to be tried before relief is obtained, and sometimes nothing but a hypodermic injection of morphine is successful. In the first place the local application of carbolic acid to the skin should be tried; a lotion of 1 in 40 may be dabbed on with a small sponge or applied on strips of lint, or a 2 per cent solution in olive oil may be employed in the same way. These applications should not be used if the skin is excoriated by scratching. Other applications are a 2 per cent solution of ichthyol, menthol in spirit (grs. viiss to the ounce), an ointment composed of equal parts of vaseline, lanoline, and boracic ointment, or the patient may take an alkaline or an acid bath, or warm douches. A bath containing nitrohydrochloric acid is given in a wooden bath, the patient remaining in it for about twenty minutes. Hypodermic injection of pilocarpine, $\frac{1}{6}$ to $\frac{1}{4}$ grain, may be employed with success. Thyroid extract has been found to give relief by Gilbert and Herscher,¹ and has been thought to act by diminishing the formation of bile acids. Nerve sedatives such as antipyrin, chloral, aspirin, and bromides give temporary relief, but their depressing effect renders the patient less able to bear subsequent itching. For itching of the skin and haemorrhages the administration of chloride or lactate of calcium in 15- or 20-grain doses may be tried three times a day for two or three days, but not longer at a stretch, as its effect in promoting coagulation of the blood is lost after a comparatively short time. Before an operation on a jaundiced patient it is well to give calcium lactate and magnesium lactate so as to diminish the risk of bleeding from the jaundiced tissues. Hypodermic injection of fresh blood serum has been employed as a prophylactic against haemorrhage (Leary,² Meyer³).

Milk is the most satisfactory food in the early stages and as long as jaundice is progressive, since it is easily digested, minimises intestinal putrefaction and fermentation, and acts as a diuretic. The patient's inclination should be consulted, and when appetite returns, rusks, ~~bread~~,^{df} toast, jam, sago, tapioca, boiled rice, potatoes (preferably mashed), pounded fish, kedgeree, pounded chicken, chicken cream, and a little meat may be given. Fatty food, for which jaundiced patients often have a marked distaste, should be avoided. Aleoholic drinks should be forbidden in ordinary jaundice, but are useful in malignant disease.

Even in inoperable malignant disease, such as carcinoma of the head of the pancreas, surgical measures may give some relief by removing the jaundice. Cholecystenterostomy, or uniting the gall-bladder to the small intestine, allows the bile to enter the intestine and thus removes the jaundice, prevents the occurrence of biliary toxæmia or cholaemia, and

¹ Gilbert et Herscher. *Compt. rend. Soc. Biol.*, Paris, 1902, liv, 1087.

² Leary. *Boston Med. and Surg. Journ.*, 1908, clix, 73.

³ Meyer. *Trans. Am. Surg. Assoc.*, 1911, xxix, 442.

greatly improves the patient's condition for a time. The operation must be performed early; if "black jaundice" has already developed, the patient is in a very unfavourable state for this procedure.

JAUNDICE IN THE NEWLY BORN

JAUNDICE occurring within a few days or weeks of birth has such special bearings that it requires separate consideration. The term *icterus neonatorum* has been specially employed for the simple jaundice so commonly seen within a few days of birth. Various forms of jaundice may attack newly born infants.

As many as nine varieties have been tabulated by Skormin; (i) Benign jaundice; (ii) septic, due to umbilical infection; (iii) infective jaundice; (iv) Winckel's disease; (v) catarrhal jaundice; (vi) toxic jaundice, due to drugs, such as carbolic acid, resorcin; (vii) jaundice following haemorrhages into the skin; (viii) jaundice of acute yellow atrophy; (ix) various forms of obstructive jaundice.

Some of the forms are extremely rare; thus, Skormin¹ could only refer to seven examples of acute yellow atrophy in infants. From a practical point of view jaundice in infants may be conveniently divided into two main groups: (i) Those which are mild and tend to recover; (ii) the severe forms in which the prognosis is grave.

THE MILD FORMS OF JAUNDICE IN THE NEWLY BORN are: (a) Idiopathic, simple, or physiological jaundice. (b) The mild infective or catarrhal.

(a) Idiopathic, Simple, or Physiological Jaundice.—*Etiology*.—It is commoner among the poor, and is known under the name of the "yellow gum." It is thought to be more frequent in premature ~~and~~ ^{small} feeble infants with deficient resistance, and has been said to be commoner in males than in females (J. L. Steven), but this is doubtful. It has been suggested that if the cord is ligatured late, so that the infant obtains a maximum of placental blood, icterus, presumably depending on increased haemolysis, is more likely to result.

Bauzon,² however, from a consideration of 240 cases, concluded that, far from favouring the occurrence of jaundice, delayed ligation of the umbilical cord improved the resistance of the infant and thus tended to prevent icterus. ^

There is no proof that delayed birth or abnormal presentations, such as a breech, are important factors.

Jaundice so soon after birth has naturally been thought to depend on events special to birth and the first few days of independent existence.

¹ Skormin. *Jahrb. f. Kinderh.*, 1902, lvi, 200.

² Bauzon. *Méd. inf.*, Paris, 1894, i, 307.

^ (Murray)

and Murray conference

Murray, F. Bot. Ind. Jour., 1922, 1, 919

It usually appears on the first or second day, rarely later; the later it occurs, the slighter the jaundice. The ~~usual~~ average duration is a week.

Birch-Hirschfeld thought it might be due to vascular engorgement of the liver causing oedema of the portal spaces, and thus pressure on the bile-ducts. The post-mortem observations of Cohnheim did not support this view. Moreover, oedema of the portal spaces, though it may be associated with jaundice, for example, when there is a tumour pressing on the bile-ducts and lymphatic vessels, does not induce jaundice. Quinke¹ suggested that, owing to patency of the ductus venosus, bile absorbed from the intestine and on its way to the liver passed from the portal vein directly into the inferior vena cava and so into the general circulation.

It is tempting to associate the microbe invasion of the previously sterile intestine with the appearance of jaundice, especially as the bile is often very viscid. There is another factor which, when taken in conjunction with infection of the alimentary canal, may help to account for icterus neonatorum. In the newly born there is an increased number of red blood-corpuscles (polycythaemia) and a correspondingly increased haemolysis. This would normally lead to an increased production of bile, and if, from microbial activity, there was even slight inflammation of the ducts, diffusion of bile into the lymphatics and jaundice would readily result.

Morbid Anatomy.—When such a jaundiced child dies from accident or from other disease, there is widespread staining of the organs and tissues of the body with the exception of the liver, kidneys, and spleen. It is remarkable that the cerebrospinal fluid, parts of the brain, and cartilages which are not stained by bile-pigment in ordinary jaundice are distinctly coloured by the bile. The lenticular and other nuclei in the brain are bile-stained ("Kernicterus") while the cortex escapes. The liver cells contain a good deal of bile-pigment, but there are no other changes; the ducts are normal, and bile can be squeezed from the gall-bladder into the duodenum. The bile is sometimes peculiarly viscid (Still²). The pericardial fluid contains bile acids and bile-pigment, shewing that there is true jaundice. The kidneys, as is commonly the case in the newly born, shew masses ("infarets") of uric acid in the collecting tubules.

Incidence.—It occurs in from 30 to 80 per cent of infants. It is said to be more frequent in lying-in hospitals than in private life. But Holt's³ figures from the Sloane Maternity Hospital of 900 births with 300 cases of jaundice (intense in 88, mild in 212) give about the lowest incidence. Steven,⁴ by adding up various statistics, found that it occurred 1212 times in 2086 children, or in 58.1 per cent. In 248 newly born infants examined by Porak⁵ it occurred in 80 per cent. *This has been stated to be commoner in males.*

Clinical Characters. ~~It comes on within the first four days of life, most commonly on the second or third day, and lasts from one to two~~

¹ Quinke. *Arch. f. exper. Path. u. Pharmak.*, 1885, xix, 34.

² Still, G. F. *Clin. Journ.*, Lond., 1901, xvii, 323.

³ Holt, E. Quoted by Osler, *Practice of Medicine*, p. 538, 5th ed., 1905.

⁴ Steven, J. L. *Glasgow Med. Journ.*, 1897, xlvii, 4.

⁵ Porak. *Rev. mens. de méd. et chir.*, Par., 1878, ii, 342.

weeks. In some instances it persists longer, and after arousing a suspicion that there is some more serious factor at work, eventually passes away. After its appearance it increases both in extent and in intensity for about a couple of days and then gradually diminishes. There are no symptoms whatever—the temperature, pulse, appetite, and faeces are normal. The urine is free from bile save in exceptionally marked cases, and there is no albuminuria. The jaundice begins on the face, chest, back, and extends to the abdomen, limbs, and lastly to the hands and feet. The jaundice shews up more prominently because of the general cutaneous engorgement, and is perhaps best seen on the back; it can be distinguished from the normal redness of the infant by pressing the blood out of the cutaneous vessels when the skin remains jaundiced. The gums may be yellow. The sclerotics are not always yellow. A division has been made into the slightest cases, in which the whites of the eyes are unaffected, and those in which the conjunctivae are icteric.

Porak described three classes—(a) The staining is slight and passes away in four days, and involves the face, back, and chest, but the conjunctivae are not affected. (b) The jaundice extends to the abdomen, arms, and thighs, while the conjunctivae may or may not be affected. (c) There is universal jaundice and the conjunctivae are always involved.

It is difficult to explain satisfactorily why the sclerotics are affected later and in a less degree than the skin; exactly the reverse of what occurs in ordinary jaundice. It is possible that it may depend upon the hyperaemic state of the skin and the correspondingly large amount of blood, containing bile, that passes through the vessels of the surface of the body.

Diagnosis.—It is distinguished from the normal reddish-brown tint of the young infant by pressing on the skin and finding that the yellow discoloration remains after the vessels have been obliterated. Its short duration prevents any confusion with congenital obliteration of the ducts; in the rare instances of more prolonged simple jaundice there is an absence of the enlarged and firm liver and spleen seen in the former condition. It must be distinguished from the grave forms of jaundice, such as infection of the umbilical vein, syphilitic disease of the liver, and Winekel's disease, by the healthy condition of the patient, the absence of fever, and, indeed, of every sign or symptom except jaundice. Grave familial jaundice, which begins in the same manner, may be suspected from the history that other infants of the family have died of it.

Prognosis.—In this condition, for it cannot be called a disease, the outlook is perfectly cloudless. But in cases of jaundice in the newly born there is always the question whether the jaundice is "physiological" or whether it is the first sign of some grave organic or infective change. The prognosis of jaundice in the first few days is, therefore, very difficult in the absence of any definite diagnosis. No special form of treatment is required (*vide* also Grave Familial Jaundice, p. 572).

(b) *Catarrhal or Mild Infectious Jaundice.*—In the first few days of

The latter it occurs the number 100 (1000000)

In a case of pyloric stenosis ^{My case} under
there was varying jaundice.
during life and much adherent
mucus in the duodenum &
stomach at the necropsy.

life the alimentary canal normally becomes invaded by micro-organisms, and a mild or virulent infection may occur. The mild forms of infectious jaundice are much the same as the catarrhal jaundice of adults, and clinically no trustworthy distinction can be drawn between mild infectious and catarrhal jaundice. Many writers, however, consider that catarrhal jaundice is almost unknown in infants. Skormin¹ refers to but three recorded cases. The disease may occur in epidemics (Lesage and Demelin²) or sporadically. It may occur in the first few days of life and in breast-fed infants. It is diagnosed by the presence of gastric symptoms, loss of appetite, vomiting, diarrhoea, slight fever, drowsiness, and jaundice—which is universal. The urine contains bile pigment, but the stools are not necessarily acholic; according to Lesage the faeces are alkaline or neutral instead of acid. These authors also lay stress on the occurrence of cyanosis. Although new-born infants may be very ill with catarrhal jaundice they usually recover (J. Thomson³).

Treatment.—The infants should be kept warm, but the room should be well ventilated. Water should be freely given, and fractional doses of calomel or grey powder should be given five or six times daily.

THE SEVERE FORMS OF JAUNDICE IN THE NEW-BORN may be divided into—(1) Those due to definite obstruction or organic change. (2) Virulent infections, either local or general. (3) Grave familial jaundice.

(1) *Jaundice due to Definite Obstruction or Organic Change.*—Congenital obliteration of the ducts (p. 649) and jaundice occurring in hereditary syphilitic disease of the liver (*vide* p. 376) and bile-duct (*vide* p. 658) are dealt with elsewhere.

Gall-stones are very rare in the newly born. Still⁴ collected ten cases either in stillborn infants or infants dying within a few weeks of birth. Seven of these were jaundiced. Thomson⁵ suggests that the inflammation of the biliary tract which induces cholelithiasis in infants is probably of the same nature as that responsible for congenital obliteration of the ducts (*vide* p. 650).

(2) *Severe Forms of Infective Jaundice.*—*Umbilical Infection.*—A very fatal form of jaundice is associated with infection of the navel in the newly born. There is suppurative phlebitis of the umbilical vein. This form of pyaemia formerly gave rise to a very high mortality among infants born in lying-in hospitals, and has been prevented by cleanliness and antisepsis. ~~According to Cantlie,~~ it is very common in Hong-Kong. The infection may be conveyed from the mother and is streptococcic. At the necropsy there is suppurative phlebitis of the umbilical vein, and the liver is pale, bile-stained, of normal size, and shews areas of small-celled infiltration in the portal spaces. There may be other pyaemic

| was

¹ Skormin. *Jahrb. f. Kinderh.*, 1902, lvi, 200.

² Lesage et Demelin. *Rev. de méd.*, Par., 1898, xviii, 14.

³ Thomson, J. *System of Medicine* (Allbutt and Rolleston), 1908, iv, Part i, 98.

⁴ Still, G. F. *Trans. Path. Soc.*, Lond., 1899, i, 151.

⁵ Thomson, J. *Edin. Hosp. Rep.*, 1898, v, 1.

⁶ Cantlie. ~~*Br. J. Hygiene*, 1901, vii, 11.~~

manifestations, such as streptococcic peritonitis, pleurisy, meningitis. There may be septicaemia.

There is jaundice, accompanied by fever and evidence of suppuration at the umbilicus, which is red and swollen. Vomiting and diarrhoea are present; the respiration and pulse are rapid. The child is first restless, and then becomes cyanosed and comatose. Death may be due to umbilical or gastro-intestinal haemorrhage.

Severe Forms of Jaundice due to General Infections.—Septicaemia may give rise to toxæmic jaundice in the newly born as well as haemorrhages and haematuria. It may be sporadic, as in pyaemia secondary to suppurative arthritis or to infected epiphyseal disease in congenital syphilis.

Epidemic Forms of Severe Infective Jaundice.—Epidemics of jaundice in infants accompanied by diarrhoea, haematuria, and attended with great mortality were described by Pollak,¹ Laroyenne,² Parrot,² and Winckel.⁴ Winckel described an epidemic, which proved fatal to 23 out of the 24 infants attacked, under the name of pernicious icteric cyanosis. This disease in the newly born has been called Winckel's disease. It is regarded by Lesage and Demelin as a very severe form of infection of intestinal origin, corresponding to the mild form of infectious or catarrhal jaundice. Thomson⁵ also regards this form as of intestinal origin. It is probably a severe form of septicaemia, and closely resembles Buhl's disease, in which there are jaundice, gastro-intestinal haemorrhages, with infarcts and acute fatty degeneration of the organs of the newly born infants.

The clinical features are mainly those of a severe septicaemia occurring in epidemics among newly born infants and accompanied by haematuria and jaundice. The skin has a bronzed appearance, probably due to a combination of jaundice and the cyanotic condition of the skin. An important feature is haematuria: Winckel, however, described haemoglobinuria. The condition is extremely fatal, and treatment is practically useless. The disease differs from umbilical phlebitis in the absence of any signs of local inflammation about the navel, and in the slighter degree of fever. Treatment should be directed to removing the contents of the bowels by purgatives and enemas. Saline solution should be given subcutaneously, and diuresis favoured by giving water by the mouth. Minute doses of calomel should be given every two or three hours until eight or ten doses have been given, so as to disinfect, as far as possible, the intestinal tract.

(3) **Grave Familial Jaundice.**—~~In some recorded examples~~ successive infants become jaundiced and die. Pfannenstiel⁶ considers that the condition is not Winckel's or Buhl's disease, and regards it as an intense

¹ Pollak. *Wien. med. Presse*, 1871, xii, 458.

² Laroyenne. *Congrès pour l'avancement des sc.*, Lyon, 1873.

³ Parrot. *Arch. physiol. norm. et path.*, 1873, v, 512.

⁴ Winckel. *Deutsche med. Wchnschr.*, 1879, v, 303, 319.

⁵ Thomson. *System of Medicine* (Allbutt and Rolleston), 1908, iv, Part i, 102.

⁶ Pfannenstiel. *München. med. Wchnschr.*, 1908, lv, 2233.

or convulsions, ^{usually} with a fortnight;
in Comay; in 1920 one of us (H.R.) collected 130 cases in 25 family groups. The sex incidence is equal, the first and second children appear to escape more often than the subsequent members of the family. It had occurred in towns (still).

Still, G. F.

Hydro

Tylecote. Mcd. Chron., Manchester,
1914, LViii, 465.

Rolliston. Practitioner, 1920, CIV, 1

Morris Austral med. Soc., 1911, NSI, 149

form of physiological jaundice of the newly born. Necropsy shows exudations into the serous cavities, enlargement of the liver and spleen, and punctate haemorrhages into the internal organs. All the tissues of the body are bile-stained; and although there are no nervous symptoms, there is selective staining of the lenticular and other nuclei by bile ("Kernicterus"), while the cerebral cortex is unaffected. Busfield¹ noted 9, and Auden² 8, in one family. The parents are usually healthy, ~~and a woman under my care became jaundiced during each pregnancy and had had three children, who died of jaundice at ages of two weeks, three months, and five months.~~³ ~~A similar recurrence of jaundice in the mother and in the infants has been recorded by Nason.~~⁴ In Arkwright's⁵ series of 14 cases in a family the mother had had jaundice when four years old. It may be very difficult to separate cases of this kind from congenital obliteration of the ducts in the absence of a necropsy. ~~The treatment is the same as in severe infective jaundice of the new-born, but it may be worth while to treat the mother during pregnancy with~~ ~~urotropin and salicylate of sodium, and small doses (½ gr.) of calomel, and a lacto-vegetarian diet.~~

but in the families recorded by Nason, Tytlocote, and Rolleston, the mothers had recurrent jaundice in their pregnancies. The infants should be given minute doses of calomel.

~~hexamine~~ Hereditary Jaundice.—Jaundice is hereditary in certain conditions, such as simple family cholaemia (*vide* p. 40), chronic splenomegalic haemolytic jaundice (*vide* p. 537), grave familial jaundice, occasionally in hypertrophic biliary cirrhosis (Boinet,⁶ Boix⁷), and in some allied anomalous cases (Lortat-Jacob and Sabaréanu,⁸ Barlow and Shaw⁹). In addition, some patients have life-long jaundice without any splenic enlargement; the condition resembles the congenital form of chronic splenomegalic haemolytic jaundice, especially in the remarkable freedom from symptoms (Glaister,¹⁰ Cocking,¹¹ A. Pick¹²). It has been suggested that such cases may be due to some abnormalities in the bile ducts, or intra-uterine obliterative cholangitis in the liver (Weber¹³), or that there is a congenital communication between the intrahepatic bile-ducts and the lymphatics (Pick).

ICTERUS GRAVIS

ICTERUS GRAVIS, or malignant jaundice, is somewhat loosely used for cases of severe toxæmic jaundice which tend to end fatally and shew

¹ Busfield. *Brit. Med. Journ.*, 1906, i, 20.

² Auden. *St. Barth. Hosp. Rep.*, 1905, xli, 139.

³ Rolleston. *Brit. Med. Journ.*, 1910, i, 864.

⁴ Nason. *Ibid.*, 1910, i, 989.

⁵ Arkwright. *Edin. Med. Journ.*, 1902, N.S., xii, 156.

⁶ Boinet. *Arch. gén. de méd.*, Paris, 1898, clxxxi, 385.

⁷ Boix. *Compt. rend. Soc. Biol.*, Paris, 1898, i, 297. f.c

⁸ Lortat-Jacob et Sabaréanu. *Rev. de méd.*, Paris, 1904, xxiv, 810.

⁹ Barlow and Shaw. *Trans. Clin. Soc.*, Lond., 1902, xxxv, 155.

¹⁰ Glaister. *Lancet*, Lond., 1879, i, 295.

¹¹ Cocking. *Quart. Med. Journ.*, Sheffield, 1903, xi, 104.

¹² Pick, A. *Wien. klin. Wchnschr.*, 1903, xvi, 493.

¹³ Weber. *Edin. Med. Journ.*, 1903, xiv, 111.

extensive degeneration of the liver cells. It thus includes a number of different conditions, such as the most severe cases of febrile jaundice or Weil's disease, acute yellow atrophy of the liver, phosphorus and other forms of mineral poisoning, and other cases in which an acute toxæmic or infective condition of the body falls on the liver and gives rise to widespread acute degenerative and necrotic changes in the liver cells; for example, in yellow fever and in streptococic and staphylococic hæmic infections. The term *icterus gravis* may also appropriately be applied to cases in which acute degenerative changes are superimposed on some pre-existing disease of the liver, such as cirrhosis or nutmeg liver. *Icterus gravis* should, therefore, be regarded not as a specific disease, but as a group of symptoms, due to the rapid development of hepatic insufficiency, eventually becoming absolute, which may be due to many different causes.

Icterus gravis may be divided into—(a) Cases in which the liver was previously healthy, in phosphorus poisoning, acute yellow atrophy, and yellow fever. (b) Cases in which it supervenes as a terminal lesion on pre-existing hepatic disease—*e.g.* in cirrhosis or chronic venous engorgement. Boix's¹ classification, though based on different grounds, is much the same :

Specific and primary <i>icterus gravis</i> :	{	In phosphorus poisoning.
		In yellow fever.
		Essential (acute yellow atrophy).
Non-specific and always secondary :	{	In staphylococic and streptococic infections.
		In infection with the colon bacillus.

Acute yellow atrophy is a special form of *icterus gravis*. The terms *icterus gravis* and acute yellow atrophy are not absolutely synonymous, for all cases of *icterus gravis* do not shew the naked-eye appearance of acute yellow atrophy, though the change—acute degeneration in the liver cells—is essentially the same in both. Under the microscope the appearances are so closely allied that from a pathological point of view they may be said to pass into each other. Cases of acute yellow atrophy are often described as *icterus gravis*, and, conversely, cases of *icterus gravis* are sometimes reported under the heading of acute yellow atrophy.

Since some of the various conditions, such as acute yellow atrophy, phosphorus poisoning, and Weil's disease, which are or may be included under the generic term *icterus gravis*, will be separately described, the clinical features of *icterus gravis* will not require any further description than that found under the heading of acute yellow atrophy. Generally speaking, the liver is somewhat enlarged in *icterus gravis* and the degenerative changes are not so uniform or so markedly necrotic as in acute yellow atrophy. The morbid changes described under the heading of Acute Hepatitis may be present in *icterus gravis*, or in some instances very

¹ Boix. *Manuel de médecine*, edited by Debove and Achard, vi, 342.



extensive fatty change (*vide* p. 428). In icterus gravis due to staphylococcic and streptococcic infection the temperature is raised, while in other instances the temperature is, as in phosphorus poisoning, depressed.

Multiple Non-Inflammatory Necrosis of the Liver.—Probably this is the best place to refer to a condition described by Oertel,¹ who could not assign it to any known disease of the liver; subsequently² he recorded a case of chronic venous engorgement terminating with this change. Under the title of "*Multiple non-inflammatory necrosis of the liver with jaundice* (Hepar necroticum cum ictero)" he described a peculiar cellular destruction of the hepatic cells, unaccompanied by inflammatory reaction or coagulation-necrosis. The process was most marked in the centre of the lobules, the cells shewing fatty change and infiltration with bile. The liver is not diminished in size to any extent, but appears tough and bile-stained. The process was regarded as due to cytotoxicity caused by autolytic ferments. Clinically the condition was one of intoxication with stupor, jaundice, delirium, and coma. Curschmann³ had previously described 2 cases as a "peculiar form of necrosing hepatitis," and Parkes Weber⁴ employed the title "disseminated lobular necrosis of the liver with Jaundice." Churchman⁵ recorded febrile cases with jaundice resembling intermittent hepatic fever.

ACUTE YELLOW ATROPHY

Necrosis, Acute

Synonym: Acute Atrophy of the Liver.

Definition.—An acute, probably autolytic, necrosis of the liver cells with diminution in the size of the liver, accompanied by jaundice, fever, nervous symptoms, and usually a fatal termination.

The history of acute yellow atrophy has been exhaustively investigated by J. Wickham Legg.⁶ The earliest case that he has unearthed is one by Baillou (Ballonius), who died in 1616. Bright,⁷ in 1836, described the condition as due to acute inflammation, and gave a good coloured drawing of the liver, and Rokitansky gave it the name "acute yellow atrophy" in 1842. called

Incidence and Etiology.—That the disease is rare is shewn by the fact that among 21,682 medical cases at the Johns Hopkins Hospital, Baltimore, there were only 3 examples (Thayer⁸). Some observers, however,

¹ Oertel, H. *Journ. Exper. Med.*, N.Y., 1906, viii, 103.

² Idem. *Arch. Int. Med.*, Chicago, 1910, vi, 293; *Berlin. Klin. Wochenschr.*, 1912, xlix, 2019.

³ Curschmann. *Deutsche Arch. f. klin. Med.*, Leipz., 1899, lxiv, 564.

⁴ Weber, F. P. *Proc. Roy. Soc. Med.*, 1909, ii (Path. Sect.), 109.

⁵ Churchman. *Ann. Surg.*, 1911, liii, 783.

⁶ Wickham Legg. *Bile, Jaundice, and Bilious Diseases*, p. 416, 1880.

⁷ Bright, R. *Guy's Hosp. Rep.*, 1836, i, 613.

⁸ Thayer, W. S. *Bull. Johns Hopkins Hosp.*, Balt., 1908, xix, 50 and private letter.

have met with a succession of cases in quite a short time. Reiss saw 5 cases in three months and Arnold 4 in a similar period.

In twenty-seven years I have seen in the post-mortem room or examined the livers of 14 cases.

Up to 1895 W. Hunter¹ was able to refer to only 250 published cases, and in 1903 Best² collected 450 cases. In twenty-five years 7 cases occurred at St. Bartholomew's Hospital, which, according to Brunton and Tunnicliffe,³ is 1 in every 500,000 applications for treatment at that charity. In twenty-seven years there were 11 cases brought to necropsy at Guy's Hospital (Hilton Fagge⁴).

Age.—It is commonest between the ages of twenty and thirty. According to Hunter's figures, half the cases occur in this decade, and four-fifths between the ages of ten and forty. A certain proportion—I have collected 42 such cases—occur within the first ten years of life; while in rare instances it has been seen within the first year or even shortly after birth.

Skormin⁵ refers to 7 published instances of acute yellow atrophy in newly born infants.

Subacute atrophy (*vide* p. 583) is relatively more frequent in children, probably from their greater power of repair. In connexion with the occurrence of cases in very early life the resemblance between some cases of icterus gravis and rather rapid intercellular cirrhosis of hereditary syphilis must be borne in mind.

The youngest case in which I have had the opportunity of cutting sections of the liver was in a child aged two years; the liver weighed 11 ounces, and shewed the naked-eye and microscopic appearances of acute yellow atrophy. I am indebted to the late Dr. Schorstein and Dr. O. Grünbaum for the liver of this case.

Sex.—Among adults females are more often attacked than males, the proportion between the two being nearly 2 to 1. In children the incidence appears to be reversed; in 34 cases collected by Phillips⁶ there were 25 males and 9 females. The greater incidence of the disease in women seems to depend on a special association between pregnancy and this disease. The influence of *pregnancy* is borne out by the large proportion of the cases in connexion with this event. The liver appears to be peculiarly susceptible to morbid changes during pregnancy, and there is reason to believe that necrotic changes in the peripheral zone of the lobules of the liver play a very important part in the production of puer-

¹ Hunter, W. Allbutt's *System of Medicine*, 1897, iv, 102.

² Best. *Thesis*, Chicago, 1903. Quoted by Kelly, *System of Medicine* (Osler and McCrae), 1908, v, 718.

³ Brunton and Tunnicliffe. *St. Barth. Hosp. Rep.*, 1896, xxxii, 436.

⁴ *Principles and Practice of Medicine*, edited by Pye-Smith, vol. ii. p. 544, 4th ed., 1902.

⁵ Skormin. *Jahrb. f. Kinderh.*, 1902, lvi, 200.

⁶ Phillips. *Amer. Journ. Med. Sc.*, Phila., 1912, exliii, 177.

Y. A. M. W.

A/LEYTON

Emotional jaundice during pregnancy
(Rouvier and LAFFONT) or in the course
of syphilis may pass into acute atrophy.

Taken in piece of small
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ROUVIER et LAFFONT. Bull. Soc. d'obstet. et de gyn.
de Paris, 1912; i, 383.

peral eclampsia. Williams,¹ who collected 12 cases of the pernicious vomiting of pregnancy shewing acute yellow atrophy, insists on a distinction between eclampsia, in which necrosis occurs in the peripheral zone, and acute yellow atrophy, in which necrosis begins in the intermediate zone of the lobule.² Acute yellow atrophy usually occurs in the second half and after the seventh month of pregnancy.

Mental disturbance, shock, or fright has preceded the onset of the disease in a certain number of cases. The mental worry in persons with syphilis or in women ~~that are~~ (pregnant), especially if unmarried, may ~~and~~ further ~~to~~ depress the resistance of the body and ~~to~~ dispose to the disease. A/SO

In recording 6 fatal cases of acute yellow atrophy of the liver in Australia Hardie³ attached importance to the anxiety with which women look forward to parturition in hot climates.

Syphilis.—The secondary stage of syphilis may be accompanied by jaundice, which is usually harmless and yields to specific treatment (*vide* p. 349). In rare instances acute yellow atrophy supervenes. This is more often seen in women than in men. The effect of the syphilitic infection would appear to fall on the liver acutely, just as it sometimes does on the spinal cord, giving rise to acute myelitis. As examination of the liver in 5 cases failed to shew the *Treponema pallidum*, it is probable that the acute atrophy is due to poisons manufactured elsewhere by the *Treponema pallidum* and carried to the liver, and so is analogous to delayed chloroform poisoning (Fischer⁴). M'Donald⁵ suggests that syphilis merely reduces the resistance of the organ and thus enables a poison formed in the intestine to set up acute yellow atrophy. Other hypotheses have been put forward (*vide* Weber⁶), such as its dependence on the autolytic action of mercury, which seems unlikely in view of its occurrence in cases in which that drug has not been given.

In 72 cases of acute yellow atrophy syphilis was noted as a causal factor in 7 (Lebert⁷). In 1909 Weber estimated that there were 53 cases of acute yellow atrophy in secondary syphilis on record; out of 50 collected cases there were only 10 males (Fischer). In some cases the jaundice has run a long course, and although the morbid appearances are like those of acute yellow atrophy, it is probable that for a considerable time the jaundice is due to intercellular cirrhosis and that a terminal and acute necrosis of the liver cells supervenes. This would place these cases in the category of icterus gravis.

Hilton Fagge⁸ drew attention to the resemblance between the appearances

¹ Williams, J. Whitridge. *Johns Hopkins Hosp. Bull.*, Balt., 1906, xvii, 71.

² Compare Opie. *Trans. Assoc. Am. Phys.*, 1904, xix, 132.

³ Hardie, D. *Austral. Med. Gaz.*, Sydney, 1889-90, ix, 179.

⁴ Fischer, W. *Berlin. klin. Wchnschr.*, 1908, xlv, 905.

⁵ M'Donald. *Edin. Med. Journ.*, 1908, N.S., i, 83.

⁶ Weber, F. P. *Proc. Roy. Soc. Med.*, Lond., 1909, ii (Path. Sect.), 113.

⁷ Lebert. *Virchows Arch.*, 1854, vii, 383.

⁸ Hilton Fagge. *Trans. Path. Soc.*, Lond., 1867, xviii, 136.

omit, as
probably
irrelevant.

of intercellular cirrhosis and those in a case of acute atrophy supervening on the secondary syphilis.

d/ As already mentioned, the mental anxiety caused by syphilis has been thought to play a part in the production of acute atrophy.

u/ Talamon¹ described a case in which a severe fright in a girl aged seventeen, who had secondary roseola, enlarged glands, and condylomas at the time, was followed within eighteen hours by "emotional jaundice"; this lasted three weeks, and symptoms of acute yellow atrophy, haemorrhages, delirium, and convulsions carried her off on the twenty-ninth day. The liver shewed acute parenchymatous and interstitial inflammation. In this case the emotional jaundice seems to have rendered the liver more susceptible to the syphilitic toxin.

The following case, for which I am indebted to Dr. A. H. Wilson, illustrates some of the features of acute yellow atrophy due to syphilis. A girl aged seventeen, with a sore on the right labium and a roseolous rash, became jaundiced six weeks before death. Three days later she began to vomit and continued to do so until her death; at no time was there blood in the vomit. Three weeks before death jaundice increased, her mental condition was affected, delirium supervened, and the urine and faeces were passed involuntarily. She became extremely hungry and thirsty. She was admitted to the South Devon and East Cornwall Hospital in a state of collapse twenty-four hours before her death. There were bile-pigment, leucine, and tyrosine in the urine. She died comatose. The liver, which I examined microscopically, shewed haemorrhages, intercellular cirrhosis, and acute necrosis of the cells.

Preceding Infective Disease.—The disease has been noticed to supervene very shortly after some infectious disease, such as influenza (Miller and Hayes²), enteric fever (George³).

Alcoholic excess in a few instances has apparently stood in a causal relation to acute yellow atrophy, since the disease has been noted to come on after recent and undoubted excessive indulgence.

Thierfelder,⁴ refers to 6 such cases among his 143 cases of acute atrophy, and cases have been described by Moxon,⁵ Cayley,⁶ Carrington,⁷ Musser.⁸

Acute yellow atrophy may occur in chronic drunkards, and acute atrophy has been described as supervening on existing cirrhosis. Thierfelder quotes 8 cases of this kind. It must, however, be borne in mind that cases of protracted acute atrophy may shew some recent fibrosis. Inasmuch as alcohol is a protoplasmic poison, it is not improbable that the resistance of the liver being diminished by alcoholic excess, other

¹ Talamon. *Méd. mod.*, Paris, 1897, viii, 97.

² Miller and Hayes. *Journ. Path. and Bacteriol.*, Cambridge, 1909, xiii, 53.

³ George. *Inaug. Diss.*, Freiburg, 1899. Quoted by Miller and Hayes.

⁴ Thierfelder. v. Ziemssen's *Cyclopaedia of the Practice of Medicine*, 1880, ix, 245.

⁵ Moxon. *Trans. Path. Soc.*, Lond., 1872, xxiii, 138.

⁶ Cayley. *Ibid.*, 1883, xxxiv, 127.

⁷ Carrington. *Ibid.*, 1885, xxxvi, 221.

⁸ Musser. *Am. Journ. Med. Sc.*, 1884, lxxxviii, 166.



In rare instances ether
may produce the symptoms
of delayed chloroform
poisoning. | ^

In trinitrotoluene ^{and} tetrachlorethane the
changes of acute atrophy may occur.
PAULY has briefly reported acute atrophy
ascribed to melinite which contains
picric acid.

PAULY Lyon med., 1917, CXXVI, 61

causes making for acute yellow atrophy are thus enabled to become effective.

Chloroform Narcosis.—Wells¹ recognises two forms of delayed chloroform poisoning—(a) with fatty change in the periphery of the lobules, acid intoxication, and no jaundice (*vide* p. 428); (b) resembling acute yellow atrophy. The latter is so rare that additional factors, such as infection and diminished resistance of the liver, must be necessary to explain its occurrence. Experimentally a change closely resembling acute yellow atrophy in man has been obtained by the combined action of chloroform and bacteria (*B. coli*, *Streptococcus pyogenes*) on the liver (Opie²).[^]

Max Ballin³ collected 9 fatal cases of acute yellow atrophy after operations. It has also been reported after narcosis by anaesthol, which consists of chloroform, ethyl chloride, and ether (Torek⁴).

The Influence of Pre-existing Hepatic Disease.—The lesions of acute yellow atrophy may supervene in the course of diseases of the liver, such as cirrhosis, catarrhal jaundice, chronic venous engorgement, or gall-stone obstruction. The onset is, no doubt, favoured by the morbid condition of the organ. In these cases it is more convenient to describe the condition as icterus gravis rather than as acute yellow atrophy. Impaired vitality and resistance on the part of the liver must render it more susceptible to acute infectious or toxic influences, and so to acute atrophy. This very probably accounts for the influence of pregnancy in disposing to acute yellow atrophy. Probably metabolic disturbances may render the liver so susceptible that streptococci are enabled to induce acute atrophy (Opie). The occurrence of such a rare disease in two sisters (Graves⁵), and in a brother and sister (Griffin⁶), suggests that congenital want of resistance may be a factor of importance.

Relation to Phosphorus Poisoning.—Inasmuch as there is a marked resemblance between the clinical features of acute yellow atrophy and phosphorus poisoning, and since the nature of the change in the liver cells is essentially the same, namely, one of acute necrosis with antolysis, it has been thought that all cases of acute yellow atrophy are due to phosphorus poisoning. In support of this it might be urged that examples of what were for a time considered undoubted instances of acute yellow atrophy have on further enquiry turned out to be due to phosphorus poisoning. Poore,⁷ who quoted cases of this kind, unhesitatingly believed that clinically and pathologically the two conditions are indistinguishable.

Generally speaking, however, the differences between the two con-

¹ Wells, H. G. *Arch. Int. Med.*, Chicago, 1908, i, 594.

² Opie. *Journ. Exper. Med.* N.Y., 1910, xii, 385.

³ Max Ballin. *Ann. Surg.*, 1903, xxxvii, 362.

⁴ Torek. *Ibid.*, 1910, lii, 489.

⁵ Graves. *Clinical Medicine*, p. 459, 1843.

⁶ Griffin. *London Med. Gaz.*, 1834, xiii, 801.

⁷ Poore, G. V. *Nervous Affections of the Hand and Other Clinical Studies*, p. 166, 1897.

ditions are sufficiently definite to separate them, and we are certainly not justified in assuming that all cases of acute yellow atrophy are due to phosphorus poisoning. These differences are—(1) In acute yellow atrophy the diminution in size is practically constant, whereas in phosphorus poisoning enlargement is the rule. (2) In acute yellow atrophy the changes in the liver cells lead to rapid disintegration with but slight increase in the amount of fat; while in phosphorus poisoning there is very extensive fatty metamorphosis of the liver cells, the amount of fat in the organ reaching 30 per cent as against 5 per cent in acute yellow atrophy.

According to Schmaus,¹ however, these differences are merely a matter of time, and as death occurs more rapidly in phosphorus poisoning, there is not time for the absorption and removal of fatty and degenerative products. When life is prolonged, the condition resembles that of acute yellow atrophy.

It may be safely stated that they are closely allied forms of icterus gravis, but at present, for purposes of clinical practice, it is convenient to regard them as distinct.

Morbid Anatomy.—An account will first be given of the changes in the ordinary acute cases, and then the changes in the prolonged cases of subacute atrophy will be described. The liver is diminished in size; in fact, cases otherwise resembling acute atrophy, in which the organ is large, belong to the allied condition of icterus gravis, for diminution in size is an essential part of acute yellow atrophy. It may weigh half or a third of its normal weight. Twenty-eight ounces is not uncommonly found instead of the normal (53 ounces in males, 45 ounces in females). Reichmann² recorded a weight of 21 oz. (593 grams) in a boy aged seventeen years. The atrophied condition is usually universal, but the left lobe is often in a more advanced state than the remainder, and the change is often thought to begin there.

The surface is smooth, and from atrophy of the liver the capsule is wrinkled and loose, so that it can be picked up by the fingers, like the walls of a half-filled bladder. If a stream of water is turned on to the organ, the capsule is thrown into folds and wrinkles. It can be peeled off quite easily in many cases. Externally the organ has a greenish-yellow colour, often relieved by red splashes. There may be small haemorrhages under the capsule. The liver is flabby and limp, and collapses and bends under its own weight; thus it readily doubles over on itself and is without the rigidity of a normal liver. If kept for some time, the surface of the liver may become covered with a white efflorescence which is composed of crystals of leucine and tyrosine.

On section of the organ the surface is bright yellow usually with reddish-brown areas. As a rule, there is more of the yellowish change, but in some rare examples of what have been called acute red atrophy,

¹ Schmaus. *A Textbook of Pathology and Pathological Anatomy*, p. 396. American translation, 1903.

² Reichmann. *München. med. Wchnschr.*, 1908, lv, 959.

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Kahn and Barsky found that the water content was high thus differing from the liver necrosis induced by phosphorus or chloroform poisoning

diffuse red atrophy greatly predominates or is universal. The yellow areas are softened and swollen, and the red areas firmer and cut like collapsed lung. The yellow colour is due to bile and not to fat. In the red areas the change is older than in the yellow areas. The longer, therefore, the patient lives, the greater will be the extent of the red change found after death. The only exception to this general statement is that in subacute atrophy, in which compensatory hyperplasia has taken place, there are nodular masses composed of proliferating liver cells which may be yellow, green, or white, and contrast with the surrounding red atrophy. In the areas of red atrophy absorption of the necrotic cells and of fat has taken place, and the only tissue left is the fibrous matrix and the capillaries which account for the red colour. Red atrophy is thus a further stage of the yellow atrophy and not an independent change. The areas of red atrophy are sunken and depressed below the level of the yellow areas. It is often more marked in the left than in the right lobe.

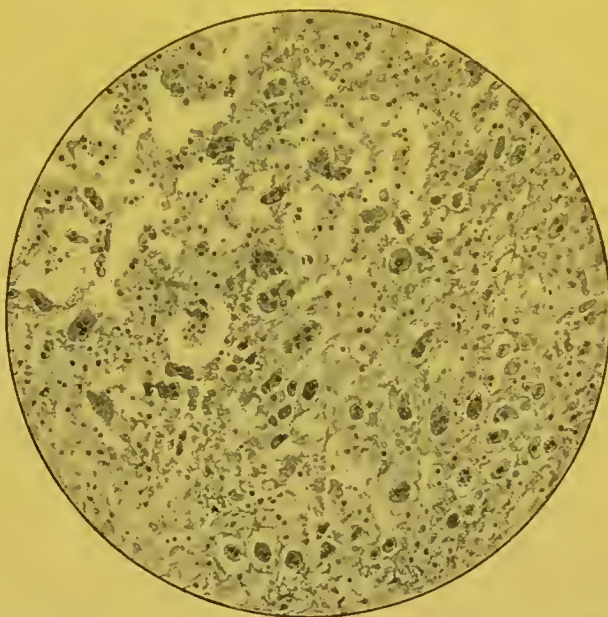


FIG. 79.—Drawing of microscopic section of the liver in acute yellow atrophy. Many of the cells are destroyed, the nuclei of some only remaining in the debris. There are, in addition, groups of liver cells and some with two or three nuclei—evidence of regeneration. $\times 140$.

The outlines of the lobules are lost in the red areas, and with difficulty, if at all, discernible in the yellow areas; if visible, they are much smaller than in health. The gall-bladder contains bile, often thick from mucus, but the larger bile-ducts often contain mucus only. Budd¹ described a case in which the bile was markedly acid.

Analyses of the liver by A. E. Taylor² and Wells³ shew that the amount of fat is not increased, that the amount of water is considerably increased, and that amino-acids due to autolysis are present, viz. histidine, lysine, tyrosine, leucine, glycocoll, alanine, proline, glutaminic and aspartic acids.

A scraping of the fresh section shews under the microscope degenerated liver cells, and crystals of leucine, tyrosine, and xanthine. In

¹ Budd. *Diseases of the Liver*, p. 264, 1857.

² Taylor. *Journ. Med. Research*, Boston, 1902, viii, 424.

³ Wells, H. G. *Journ. Exper. Med.*, N.Y., 1907, ix, 627.

the alcoholic extract of the liver of acute yellow atrophy that had been kept for two years Delépine¹ found Charcot-Leyden crystals. Crystals of leucine and tyrosine may be seen in fresh sections, but for satisfactory examination of the histological condition of the liver properly hardened sections are necessary. Little reliable information can be obtained from fresh sections made by the freezing method, for fresh sections exaggerate existing disorganisation of the liver.

Histologically, the appearances vary greatly in the areas attacked by the yellow and by the red atrophic change respectively, and even in

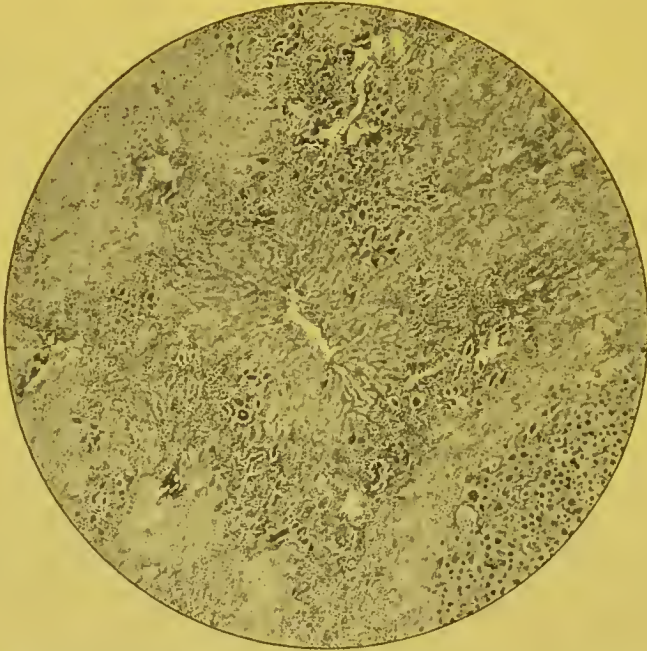


FIG. 80.—Microscopic appearances in acute atrophy of the liver. The liver cells are extensively necrosed. Around the periphery of the lobules there are small-celled infiltration and groups of liver cells. $\times 30$.

different fields of the same microscopic section. In the early stages the liver cells are swollen and may shew some fatty change, but this is not a prominent or essential change. They soon become granular, bile-stained, and shew fragmentary degeneration of the nuclei which ~~stain badly~~. Haemorrhages occur between the degenerated liver cells, and as the cells begin to undergo a further stage of necrosis, they cease to stain. Necrosis begins in the intermediate zone of the lobules, and extends towards the intralobular vein. The small bile-ducts are in a condition of cholangitis; there is proliferation of the epithelial cells, which are discharged into the lumen of the duct and by obstruction cause jaundice. Later, necrosis of the cells lining the small ducts occurs. Bile-duct-like structures are seen, especially at the margins of the lobules. In some sections the process of regeneration can be seen to be commencing in the liver cells, which are

¹ Delépine, S. *Trans. Path. Soc.*, Lond., 1891, xlii, 458.

~~order~~ become untenable before the cytoplasm

and some cases of Antrax
in children are of this
nature, especially those with
a history of previous jaundice.

collected into solid columns, so as to imitate a primitive tubular liver. These cellular strands are separated from each other by fibrillar tissue, capillaries, or the debris of the degenerated lobule. The liver cells may be much larger than natural, contain several nuclei, and may give the impression of being made up of several liver cells which have run together (*vide* Fig. 79).

In the more advanced stages—that is, in the areas of red atrophy—the cells of the lobules have completely disappeared as the result of very acute necrotic changes, and nothing can be seen except the skeleton of the lobules, formed of the fibrillar vascular connective tissue, enclosing a few nuclei and red blood-corpuscles. Sometimes the necrosis is so complete and widespread that it is difficult to recognise the tissue as liver or to make out the topography of the section. There is often, but not always, evidence of inflammatory reaction in the connective tissue. There may be a small-celled infiltration starting from the portal spaces and spreading into the peripheral parts of the lobules; a similar small-celled infiltration may also be seen around the intralobular vein.

Subacute Atrophy.—Some cases are prolonged and survive for many weeks, months, or even years; thus, in Steinhaus'¹ case the total duration was twenty-two months, and in Stroebe's² two years. In these cases, now spoken of as subacute liver atrophy, the naked-eye appearance of the liver is very different from that of the acute cases, and resembles that of nodular parenchymatous hepatitis or cirrhosis.³ Probably many cases have been described as cirrhosis with adenomas. The relation of this nodular hyperplasia to acute atrophy was probably first recognised and figured by Cayley⁴ in 1883. The liver is usually small. The surface shews nodular projections which may be white and caseous-looking, but are generally yellow, green, or brown from bile-staining. They vary in size; in exceptional cases they may be very large; Barbacci⁵ recorded one as large as the fetal head, and Milne⁶ refers to 2 cases on which laparotomy had been performed for an abdominal tumour. The nodules in the liver substance are surrounded by fibrosis and condensed liver tissue. Microscopically there is fibrosis, often intercellular; and no rigid line can be drawn between subacute atrophy and acute cirrhosis. The changes in the liver cells are described in the next paragraph.

Regenerative Changes.—Cases which do not run a very acute course shew changes in the small bile-ducts and liver cells which are regarded as regenerative and compensatory. These changes have been specially studied by Marchand,⁷ Meder,⁸ Stroebe, Barbacci, Ibrahim,⁹ W. G. Mac-

¹ Steinhaus. *Prag. med. Wchnschr.*, 1903, xxviii, 323.

² Stroebe. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1897, xxi, 379.

³ Compare *Trans. Path. Soc.*, Lond., 1892, xliii, 81.

⁴ Cayley, W. *Ibid.*, 1883, xxxiv, 127.

⁵ Barbacci. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1901, xxx, 45.

⁶ Milne. *Arch. Int. Med.*, Chicago, 1911, viii, 639.

⁷ Marchand. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1895, xvii, 206.

⁸ Meder. *Ibid.*, 1895, xvii, 143.

⁹ Ibrahim. *München. med. Wchnschr.*, 1901, xlviii, 784, 838.

Callum,¹ Muir,² Macdonald and Milne.³ Microscopically it appears that in the early stages of regeneration the surviving liver cells multiply by direct (amitotic) and also by indirect nuclear division, so that columns of liver cells are formed resembling a tubular formation; the liver cells may become much enlarged, especially around the intralobular vein, and may contain several nuclei. Sometimes this compensatory hyperplasia occurs in one-half only of a lobule, the liver cells in the remainder being too necrosed to proliferate; in this event the intralobular vein may appear at the margin of the fresh mass of liver cells. This method of regeneration of the liver cells leads to the production of hyperplastic or "adenomatous" nodules in the liver, which project above the surface of the surrounding parts. According to Macdonald and Milne regeneration of the liver cells is due solely to proliferation of existing liver cells. A number of observers (Meder, Stroebe, Ibrahim, MacCallum, Yamasaki,⁴ Adler⁵) believe that when the liver cells have been extensively destroyed, regeneration is brought about in another way. As a result of proliferation of the interlobular bile-ducts blind bile-ducts work their way into the degenerated lobule. The cells forming these projections increase in size and become like liver cells. The terminal cells in the invading masses of cells shew karyokinetic figures and are evidently proliferating. Muir admits that the bile-duct structures may form cells like liver cells, but does not attach much importance to them in compensatory regeneration. To sum up, regeneration occurs as a result of hyperplasia of the surviving liver cells, and possibly from hyperplasia of the interlobular bile-ducts by means of which cells approaching liver cells are produced.

Micro-organisms have been found in some cases, but not in others, and no definite causal connexion can be said to exist between any micro-organism and the changes found.

The colon bacillus, though often found after death, can hardly be regarded as the causal agent, as there may easily be post-mortem invasion of the organ. Streptococci, staphylococci, pneumococci, have also been reported in some cases.

Probably the toxins of various micro-organisms are capable of producing in livers rendered susceptible, for example, by toxæmia, the acute necrotic changes characteristic of acute yellow atrophy.

The *kidneys* are swollen, soft, bile-stained, and shew small hæmorrhages. Microscopically the epithelium of the tubules is degenerated. Hewitt⁶ recorded 5 cases of acute yellow atrophy with necrosis of the renal epithelium.

The *spleen* is often softened and enlarged.

In 71 cases Wickham Legg found the spleen larger than natural in 43.

¹ MacCallum, W. G. *Johns Hopkins Hosp. Rep.*, Balt., 1902, x, 379.

² Muir, R. *Journ. Path. and Bacteriol.*, Cambridge, 1908, xii, 287.

³ Macdonald and Milne. *Ibid.*, 1909, xiii, 161.

⁴ Yamasaki. *Arch. f. Heilk.*, Leipz., 1903, xxiv, 249.

⁵ Adler. *Ibid.*, 1903, xxiv, 198.

⁶ Hewitt. *Johns Hopkins Hosp. Bull.*, Balt., 1906, xvii, 272.

HAYASHI and KIBATA described a sporochaete.

HAYASHI and KIBATA. Journ. infect. Dis., Chicago, 1921, XXV, 64.

He quotes Liebermeister's statistics of 87 cases, in 56 of which the spleen was enlarged.

The *lymphatic glands* in the portal fissure and the neighbourhood may be much enlarged.

The *heart* is softened, swollen, and shews cloudy swelling. The blood, as in other toxic and infective conditions, stains the vessels and coagulates imperfectly. Haemorrhages are scattered through the body on the cutaneous, mucous, and serous surfaces. Meningeal and cerebral (Politzer,¹ Lafitte²) haemorrhages have been known to occur. Toxic changes in the vessel walls allow extravasation to take place. Brunton and Tunnicliffe point out that viperine poison has the same effect when applied locally to the mesentery of a frog.

The *gastro-intestinal tract* may be inflamed, and patchy haemorrhages or small areas of necrosis may occur. The stomach and intestines may contain altered blood, and slight ascites is not uncommon.

Pancreas.—Degenerative changes in the acini, the islands of Langerhans being unaffected, have been described by Sacquépée,³ who lays some stress on this since the pancreatic juice has been found to have the power of destroying the toxins of diphtheria, tetanus, etc.

Central Nervous System.—In addition to meningeal and cerebral haemorrhages already referred to, degenerative changes, analogous to the toxic changes seen in a more chronic form in subacute combined sclerosis and in grave anaemia, have been described by Goldscheider and Moxter.⁴

Pathogeny.—The essential factor is a very acute necrosis of the liver cells resembling that produced by bacterial toxins, with evidences of inflammation in the supporting fibrous tissue of the organ. The condition is a very acute hepatitis; subacute or protracted cases pass into acute cirrhosis. It is analogous to, but more advanced than, the toxic changes seen in the liver in phosphorus, iodoform, and arsenic poisoning.

In Germany many sheep die with jaundice, haemorrhages, delirium, and acute yellow atrophy of the liver as a result of eating certain lupins. This disease, —lupinosis,—which is not met with in man, is thought to be due to a poison—ictrogen or lupinotoxin—produced by the agency of fungi in the husks of the seeds.⁵

Flexner⁶ suggested that the lesions are due to autolysis. This view that the necrosis is due to a poison which destroys the liver cells, but does not affect their autolytic ferments which then act on the dead cells, has attracted a good deal of support (Wells,⁷ White⁸).

¹ Politzer. *Jahrb. f. Kinderh.*, 1860, iii, 40.

² Lafitte. *Bull. Soc. Nat.*, Par., 1891, lxvi, 389.

³ Sacquépée. *Arch. de méd. expér. et d'anat. path.*, Par., 1902, xiv, 485.

⁴ Goldscheider und Moxter. *Fortschr. der Med.*, 1897, xv, 529.

⁵ Vide Brunton and Tunnicliffe. *St. Barth. Hosp. Rep.*, Lond., 1896, xxxii, 425.

⁶ Flexner. *Am. Journ. Med. Sc.*, Phila., 1903, exxvi, 202.

⁷ Wells, H. G. *Chemical Pathology*, p. 441, 1907.

⁸ White, F. W. *Boston Med. and Surg. Journ.*, 1908, clviii, 729.

Quinke¹ suggested that acute yellow atrophy may be due to obstruction at the biliary papilla, allowing the pancreatic juice to digest the liver. There is as yet no proof of this speculation, which is exactly the converse of Opie's explanation of haemorrhagic pancreatitis as due to the flow of bile into the pancreatic duct (*vide* p. 750). Injection of commercial pancreatin into the common bile-duct of animals has not produced acute yellow atrophy (C. L. Best²).

Clinical Picture.—*Course.*—The disease may be divided into two stages. The first, which usually lasts five or six days, but may be prolonged for many weeks, comes on either like catarrhal jaundice with gastro-intestinal disturbance followed by jaundice, or, more gradually, with malaise. In the second stage the patient passes into a "typhoid" state and develops nervous symptoms which are of the gravest significance and should at once suggest the probability of acute yellow atrophy. This stage hardly ever lasts more than a week and is usually limited to three days.

Duration.—More than half the cases, as shewn by Thierfelder and Hunter's statistics, run their course within two weeks. Cases, however, certainly occur in which the disease is spread over many weeks, months, or even up to two years. The cases have been divided into acute and subacute, according to their duration and severity. The prolonged cases may resemble obstinate catarrhal jaundice until the nervous symptoms develop, the long course of the disease being due to prolongation of the earlier or first stage. But in rare instances partial recovery may occur after acute symptoms have appeared, the patient remaining jaundiced.

The *onset* is usually insidious, and may be that of ordinary catarrhal jaundice; in a minority, about one-third, of the cases the patient suffers from indefinite illness and malaise for some time before jaundice appears. As a rule, during the *first stage* there is little or nothing to distinguish the disease from ordinary catarrhal jaundice. Fever, malaise, vomiting, constipation, bilious urine, and not uncommonly muscular pains are present. Vomiting may be very persistent and severe.

Jaundice, which is usually the first definite sign, varies in different cases: it may gradually become more marked, or it may, in prolonged cases, first fade and then become more intense before death. In some instances it may be less marked at the termination than earlier in the disease. It ^{is} due to obstruction in the smaller bile-ducts, the result of inflammatory lesions in their walls produced by the same poison that is responsible for the acute degenerative changes in the liver cells. In some exceptional cases there is no jaundice.³

This was so in a case, subsequently published by Sir L. Brunton and Dr. Tunnicliffe,⁴ which was under my care when I was House Physician at St.

¹ Quinke. In Nothnagel's *Encyclopedia of Practical Medicine*, "Diseases of the Liver," p. 642. American transl., edited by F. A. Packard, 1903.

² Best. Quoted by Wells and Bassoe. *Journ. Am. Med. Assoc.*, 1905, xlv, 685.

³ Bamberger. Quoted by Legg. *Loc. cit.* p. 439. Le Roy. *Lancet*, Lond., 1885, ii, 155.

⁴ Brunton and Tunnicliffe. *St. Barth. Hosp. Rep.*, 1896, xxxii, 436.

In a periperal Case which I saw
death occurred 24 hours after
Laceration was noticed.

But it is now more probably due to disordered function of the liver cells
This may be due to widespread degeneration of Kupffer's cells.

In a case seen in consultation
the temperature rose from below
93° to above 110° F just before
death.

Bartholomew's Hospital in 1889. Dr. E. T. Wilson kindly sent me the notes and liver of the following case: A woman aged thirty years, never strong, had slight haematemesis two years before, from which she recovered. On December 9, 1897, she suddenly felt pain and subsequently vomited a little blood; next day the liver dulness was diminished; slight haematemesis recurred on December 10 and 11, and melaena on December 12, 13, 14; after this date the motions, always offensive, became clay-coloured. The patient got weaker, drowsy, and died on December 28. There was never any jaundice. The urine was not tested for leucine and tyrosine. The temperature was generally between 99° and 100°, going up on two occasions to 101°, and was often below normal. At the necropsy the liver was very small, pale, firm to the touch and to the knife. The surface was smooth and lightish yellow with patches of slate colour; the edges were remarkably thin. Microscopically there was acute yellow atrophy. Gall-bladder was full of dark bile. Kidneys firm and pale. There were numerous submucous haemorrhages in the stomach, especially at the cardiac end.

The onset of the *second stage* is very definite, and is marked by a pronounced change for the worse in the general condition and especially by the appearance of nervous symptoms. Headache appears, or if present before, becomes intense. Intolerance of light is often complained of; the mental processes are affected; there are restlessness, delirium, and the patient may scream and become extremely violent. Twitching of the muscles and subsultus often occur, and general convulsions may supervene. Transient paralyses, such as squint, are sometimes noted. Apart from jaundice, the clinical manifestations may closely resemble those of meningitis. I have seen an extensor plantar response (Babinski's sign). The nervous manifestations pass into coma, in which the patient dies.

With the onset of the grave nervous symptoms vomiting becomes urgent, and the vomited matters often contain altered blood. The tongue is usually dry, brown, and tremulous, and the teeth become coated with sordes. The amount of sulphocyanide of potassium in the saliva is said to be diminished (Fenwick¹). Dilatation of the pupils has been regarded as an important sign, and has been so extreme as to suggest belladonna poisoning. The pulse becomes rapid, feeble, and of low tension. The respiratory rate tends to be increased or to become irregular and finally stertorous. The temperature varies, but is more often depressed than raised, but it may rise just before death. In a girl aged twenty under my care the temperature rose to 106° F. before death. The presence or absence of fever was correlated by Hanot² with different microbial poisons, infection with the colon bacillus leading, like phosphorus poisoning, to a depressed temperature, while streptococcal and staphylococcal infections are associated with pyrexia; but this is very doubtful. Occasionally a red rash appears, and arthritic swelling has been recorded. Petechiae and haemorrhages occur under the skin, and occasionally epistaxis, haematuria, retinal haemorrhages, and in women

¹ Fenwick. *Saliva as a Test for Diseases of the Liver*, 1889.

² Hanot, V. *Arch. gén. de méd.*, Paris, 1896, clxxvii, 77.

metrorrhagia are observed. Pregnant women abort. The faeces may be darkened by blood so as to resemble bile; in the later stage it is improbable that bile passes into the duodenum, inasmuch as after death the bile-ducts contain nothing but mucus. But as constipation exists throughout the disease, some of the faeces may contain bile excreted into the bowel at a very early stage of the disease. The dejecta are often extremely offensive. Diarrhoea is exceptional.

Liver Dulness.—At the onset of grave symptoms the liver may or may not be enlarged. The increased size in the early stages may be due to some old-standing change, but this is not the case in most instances. Whether preliminary hepatic enlargement is made out or not, percussion soon shews diminution of the liver dulness, which may progress until it completely disappears. Entire absence of the liver dulness is due to the atrophied and flabby organ falling away from the abdominal walls and allowing intestinal coils to take its place.

In an exceptional case recorded by Gerhardt¹ the hepatic dulness did not diminish, although the liver (29 ounces) was markedly atrophied. This was explained by the fact that the liver was firmly adherent to the anterior abdominal wall.

Flatulent distension of the intestines occurs and gives rise to difficulty in estimating the size of the liver. As mentioned above, coils of intestine may pass between the abdominal wall and the liver and entirely obliterate the hepatic dulness. The liver is often tender. In 100 cases collected by Legg² this was definitely noted in 35. Enlargement of the spleen has been occasionally noted. Ascites, though present in some cases after death, is masked by flatulence and rarely detected during life. Tileston³ collected 8 cases with ascites. In a case of ascites and intense jaundice recorded by Bryant,⁴ the ascites was due to chronic perihepatitis and the jaundice to acute yellow atrophy.

The *blood* shews a delayed coagulation-time, and may contain bile pigment (Neuberg and Richter⁵). The number of red blood-corpuscles is somewhat increased from concentration, and a very moderate leucocytosis has been observed (Cabot, Ewing⁶). Blood cultures have been negative in some instances (Libman,⁷ White⁸); in others the colon bacillus has been found (Vincent⁹).

Urine.—The amount is somewhat diminished; it is high-coloured from excess of bile pigment and urobilin. Bile acids are occasionally found. From degeneration of the renal cells albumin and casts are

¹ Gerhardt. *Ztschr. f. klin. Med.*, 1892, xxi, 374.

² Legg, W. *Bile, Jaundice, and Bilious Diseases*, p. 465, 1880.

³ Tileston. *Boston Med. and Surg. Journ.*, 1908, clviii, 510.

⁴ Bryant, J. H. *Guy's Hosp. Gaz.*, 1900, N.S., xiv, 147.

⁵ Neuberg und Richter. *Deutsche med. Wchnschr.*, 1904, xxx, 499.

⁶ Ewing. *Clinical Pathology of the Blood*, p. 341. 1901.

⁷ Libman. *Johns Hopkins Hosp. Bull.*, Balt., 1906, xvii, 222.

⁸ White. *Boston Med. and Surg. Journ.*, 1908, clviii, 729.

⁹ Vincent. *Semaine méd.*, Paris, 1893. xiii. 228.

The cholesterol-content of the blood is diminished.

The amino-acids leucine and tyrosine have been found
in excessive amounts in the blood (Stadie and van Slyke)

Stadie and van Slyke Arch int. Med., Chicago, 1920, XXV, 693.

according to Stedie & Van Slyke
and appear in the
urine because the
liver is so disorganized
as to be incapable of
de-ammonizing amino-
acids.

Stedie and Van Slyke. *Arch. int. Med.*, Chicago
1920, xxv, 693.

frequently present. Deutero-proteose, probably from destruction of the liver cells, is sometimes detected. There is no glycosuria. This is remarkable, and shews that glycosuria is not of any value as a sign of hepatic inadequacy (*vide p. 234*).

The total excretion of nitrogen in the urine may be much diminished, normal, or increased. The fall in the total nitrogen may be due to the diminished intake of protein; on the other hand, comparatively considerable excretion of nitrogen in some cases may depend on autolysis of the liver cells. Urea is diminished and the percentage of ammonia increased; normally ammonia accounts for about 5 per cent of the total nitrogen, but in acute yellow atrophy it may account for 20 per cent. This alteration in the relative proportions of urea and ammonia was in the past ascribed to failure of the liver to transform ammonia into urea. But it is ~~probable~~ ^{has been thought} that the increased ammonia depends on acidosis and fixation of ammonia by organic acids before the liver has a chance of transforming it into urea.

Leucine and tyrosine, to which great importance has been attached as replacing urea, are sometimes present in such quantities that they are spontaneously precipitated. In many cases, however, the urine must be concentrated to demonstrate them. Leucine appears as rounded discs, and tyrosine as needle-shaped crystals. Leucine and tyrosine are not invariably present; they may be absent in cases in which the liver is found to contain them, and one may be found without the other. They ^{possibly} have been ~~known to occur~~ in the urine in conditions other than acute yellow atrophy, such as erysipelas, enteric, small-pox, in some obscure febrile conditions, and leukaemia. ^{be} ~~Their presence, therefore, is not~~ ^{old} ~~pathognomonic of acute yellow atrophy, and their absence does not~~ ^{view} ~~exclude that disease.~~ ^{It was formerly assumed} that the presence of leucine and tyrosine was due to the degenerated liver cells failing to transform these bodies into urea. ^{was corroborated by Ginkow's observation} ~~This explanation is incorrect, for when the liver has been excluded from the circulation by ligature of the portal vein and the hepatic artery, leucine and tyrosine do not appear in the urine (Minkowski).~~ ^{at} ~~It appears that the leucine and tyrosine are derived from autolysis of the liver cells, This view is supported by the production of leucine and tyrosine during the autolysis, or the spontaneous digestion by intra-cellular ferments, of other organs, e.g. a pneumonic lung or pus.~~

Uric acid may be present in normal or even in increased quantities; from Jackson and Pearce's¹ experimental work this would appear to be due to hydrolysis of nuclear tissue during the autolysis of the necrotic tissue.

Prolonged or subacute cases are those which partially recover but subsequently relapse and die after weeks, months, or even more than a year. The existence of prolonged cases with continuous jaundice is difficult to verify, as the condition merges into acute hepatitis and cirrhosis. Macdonald and Milne² collected 19 cases of subacute atrophy, 4 of which occurred in children under ten years of age, and

¹ Jackson and Pearce. *Journ. Exper. Med.*, N.Y., 1907, ix, 577.

² Macdonald and Milne. *Journ. Path. and Bacteriol.*, Cambridge, 1909, xiii, 161.

Milne¹ has pointed out that children are specially affected. The morbid changes are described on p. 583.

The following case came under my observation at the Victoria Hospital for Children:—

A boy four and a half years old, whose mother had had one stillborn child and two miscarriages, had had pneumonia and bronchitis a year previously. Jaundice appeared five weeks and ascites two weeks before death. Subsequently haemorrhages developed, paracentesis to 25 ounces of turbid ascitic fluid was performed two days before death, which was preceded by coma. The liver weighed 13½ ounces, the surface was irregular, on the left lobe there was a raised area the size of a florin. On section the liver was somewhat tough, microscopically the appearances were those of acute yellow atrophy with regenerative changes in the adenomatous area in the left lobe. There was acute enteritis.

The clinical course of these cases is vague and variable, and the greater part of the illness resembles cirrhosis with jaundice rather than acute yellow atrophy. The spleen may be enlarged, and ascites appear towards the end.

Termination.—The “typhoid” state deepens into coma and absolute unconsciousness, with stertorous breathing and incontinence of urine and faeces.

Diagnosis.—Jaundice with severe constitutional and cerebral symptoms and diminution in the liver dulness are the main data on which the diagnosis is made.

Differential Diagnosis.—*From Phosphorus and Allied Forms of Poisoning.*—The absence of any evidence that phosphorus or other poison has been taken or vomited is important. The progressive diminution in the hepatic dulness and the fall in the amount of urea in the urine are in favour of acute yellow atrophy. The presence of leucine and tyrosine is not conclusive, as they may be absent in acute atrophy, and be present in phosphorus poisoning and in other conditions, such as typhoid fever, erysipelas, and leukaemia. In phosphorus poisoning there is an interval between the severe irritant symptoms and the onset of jaundice with severe constitutional symptoms; whereas there is no such interval between the first and second stages of acute yellow atrophy. There is more gastric irritation and less cerebral disturbance in phosphorus poisoning. \wedge

From *icterus gravis* the chief distinction is the size of the liver—diminished in acute yellow atrophy, increased in *icterus gravis*. From severe cases of acute infective jaundice the diagnosis is very difficult; in fact, the two conditions run into each other; those that recover are likely to be spoken of as infective jaundice, and those that prove fatal as acute yellow atrophy. Subacute atrophy is difficult to distinguish from acute cirrhosis; in fact there is a transition from acute atrophy to subacute atrophy and to acute cirrhosis. Hypertrophic biliary cirrhosis is not likely to be confused with acute atrophy, as the course of the

¹ Milne. *Arch. Int. Med.*, Chicago, 1911, viii, 638.

In fatal jaundice due to trinitrotoluene poisoning the liver may be reduced to half its size, in these cases the history and Webster's Test for T.N.T. illness will assist in the diagnosis.

Experimental grounds show
that a rich carbohydrate is
preferable to a protein or
fatty diet; /

disease is very chronic and the liver is greatly enlarged. According to Osler,¹ infective endocarditis has been mistaken for acute yellow atrophy.

Prognosis.—When the disease is fully declared, the prognosis is most gloomy; in fact, some doubt will always arise as to the nature of cases that recover completely. Some cases may have been examples of severe infective jaundice or Weil's disease, or of some other form of acute hepatitis. But the occurrence of subacute cases shewing regenerative changes makes it probable that the disease is not necessarily fatal.

In 1880 Wickham Legg² gave a list of 28 cases of reputed recoveries from acute yellow atrophy. In 1892 Wirsing³ could only collect 15 cases, not associated with syphilis, of recovery.

In a case under my care the diagnosis of acute atrophy and death, the patient being in a condition of coma, seemed equally certain, but recovery followed. In another similar case, seen in consultation, the patient became mentally deranged for several months, but eventually recovered.

Recovery depends on the severity of the attack and on the compensatory power of the body and especially of the liver cells. As nodular hyperplasia of the liver has been described in cases surviving for six months (Marchand⁴), a year and a half (Barbacci⁵), a year and three-quarters (Steinhaus⁶), and two years (Stroebe⁷), the possibility of permanent recovery cannot be denied. But symptoms may recur and prove fatal from degenerative changes attacking the areas of compensatory hyperplasia. Children, probably from their greater power of repair, more often shew the changes of subacute atrophy. The prognosis is therefore better in them than in adults. It is worst in pregnant women.

As in all forms of liver disease, the state of the kidneys is important. If they were previously healthy, the excretion of poisons due to the acute hepatic inadequacy will diminish the intensity of the toxæmia; but even then the outlook is very dismal, since the renal epithelium is affected by the poisons reaching them by the circulation and undergoes acute degeneration.

Treatment.—As the disease is not invariably fatal, it is important to adopt *prophylactic measures* in cases of jaundice in which acute yellow atrophy may possibly follow. Thus, jaundice in pregnant women, cases of catarrhal jaundice presenting much drowsiness or toxæmia, and jaundice during secondary syphilis, should be treated on the lines of diminishing toxæmia. In such circumstances the patients should for a time be kept in bed in a well-ventilated room, ~~and~~ the diet confined to milk and carbohydrates. The milk may be flavoured with coffee, cocoa, or tea, and may be thickened with cornflour. Three to four pints may

¹ Osler, W. *Principles and Practice of Medicine*, p. 704, 3rd ed.

² Legg, J. Wickham. *Bile, Jaundice, and Bilious Diseases*, p. 676, 1880.

³ Wirsing. *Inaug. Diss.*, Würzburg. Quoted by Albu, *Deutsche med. Wchnschr.*, 1901, xxvii, 216.

⁴ Marchand. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1895, xvii, 206.

⁵ Barbacci. *Ibid.*, 1901, xxx, 49.

⁶ Steinhaus. *Prag. med. Wchnschr.*, 1903, xxviii, 323.

⁷ Stroebe. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1897, xxi, 379.

be given daily. When digestion is difficult peptonised milk-gruel or Benger's food may be substituted in part or entirely for milk. Sugar and chocolate are of use in preventing acidosis. The patients should drink plenty of water so as to dilute the toxins and increase excretion; for this purpose alkaline mineral waters, such as Vichy or Vals, are suitable. The bowels should be kept freely open by calomel, followed by salts next morning twice a week, with cascara sagrada on the intervening days. The degree of purgation must be regulated by the progress of toxæmic symptoms. If necessary, the urinary excretion may be further stimulated by citrate of caffeine or diuretin combined with digitalis. The jaundice should be met by urotopin (gr. vii.) combined with sodium salicylate (gr. x.), and bicarbonate of sodium (gr. xv.), three times a day before food. Acids should be avoided. Intestinal antiseptics in one of the following forms may be tried: Beta-naphthol (gr. v.), naphthalene tetrachloride (gr. vii.), calomel ($\frac{1}{10}$ gr.), salol (gr. v.), acetozone (1 in 2000 parts of water) sweetened with syrup of lemon (2 oz. to 1 pint), $\frac{1}{2}$ to 1 pint daily, salicylate of bismuth (10 gr.). In the jaundice of secondary syphilis, mercurial treatment is essential.

In cases in which the onset of acute yellow atrophy seems fairly certain the above measures should be pushed, and in addition enemas or subcutaneous or intramuscular transfusions of saline solution should be carried out to obviate the toxæmia. Sodium bicarbonate should be given in larger quantities (1 dram) three or four times daily by the mouth or in the enemas or transfusions (3 drams to 1 pint). As the condition is thought to depend on autolysis of the liver, I gave horse serum, which has an anti-autolytic action, in one case which eventually recovered. Vomiting should be treated by careful feeding, small doses of cocaine, ~~dilute hydrocyanic-acid~~, or small hypodermic injections of morphine. Sleeplessness and delirium should be met by tepid sponging, ice-bags to the head, bromides, morphine, veronal, or trional. Chloral and its allies should be avoided, because the chloroform which is formed exerts a toxic action on the liver cells as shewn by delayed chloroform poisoning. The circulation should be maintained by hypodermic injections of ~~strychnine~~.

JAUNDICE OF PHOSPHORUS POISONING

Incidence.—Acute phosphorus poisoning is rare in this country; in the ten years ending 1903 there were 152 fatal cases in England and Wales. In Vienna it is commoner, and is used as a means of committing suicide by prostitutes and unmarried girls who are pregnant. When taken with suicidal intent, an emulsion of the heads of lucifer matches or of rat paste has been employed. Accidental poisoning may be due to eating rat paste under the impression that it was something else, or the flesh of animals, especially poultry, which have died from devouring





vermin poisoned by phosphorus (Poore¹), or even to the application of phosphorescent paste to the skin, and its medicinal use. In the past some writers attributed all cases of acute yellow atrophy to undetected phosphorus poisoning. A condition resembling phosphorus poisoning may be due to iodoform, arsenic, and antimony.

Morbid Anatomy.—The liver is, as a rule, much larger than natural, firm and feeling like a fatty liver, and of a pale yellow colour. In exceptional cases it has presented exactly the features of acute yellow atrophy, but the change in the liver is essentially one of increase in size due to acute fatty metamorphosis, and resembles that of delayed chloroform and of iodoform poisoning. The amount of fat in the liver is greatly increased; normally it contains about 3 per cent of fat, whereas in phosphorus poisoning it may contain 30 per cent. It thus contrasts with acute yellow atrophy in which the amount of fat is not increased. It is said that if life is sufficiently prolonged, the liver diminishes in size from absorption of the fat and so comes to be in the same condition as in acute yellow atrophy. Under the capsule and on section the yellow buff aspect of the liver substance shews here and there reddish spots due to haemorrhage, which stand up against the bile-stained liver substance.

The fat is not produced by changes in the protoplasm of the liver cells, but is brought to the liver from other parts of the body; the degenerated condition of the liver cells allows this fat to be deposited in them in very excessive quantities (Rosenfeld²).

Microscopically the liver cells shew cloudy swelling, indistinct outlines, and advanced fatty metamorphosis, especially towards the periphery of the lobules. The cells in parts of the lobules may contain granules of bile-pigment. The cytoplasm is more affected in phosphorus poisoning, whilst in acute atrophy the nucleus suffers most. Glycogen disappears from the cells. Leucine and tyrosine may also be found in the liver. There is sometimes slight proliferation of the connective tissue of the portal spaces, and in cases that recover some cirrhosis probably develops. The small bile-capillaries are blocked and obstructed (Eppinger³), thus accounting for the jaundice.

The heart usually shews fatty change, and may be so soft as to be readily perforated by the fingers during its examination. The kidneys shew an apparent fatty increase in the parenchyma, but chemical analysis proves that there is no real increase. The voluntary muscles also undergo fatty change. The spleen may be much enlarged. Haemorrhages are scattered throughout the body.

Pathogeny.—The hepatic changes in phosphorus poisoning are thought to depend on aseptic autolysis due to autolytic ferments, one of which is probably arginase (Wakeman⁴); for Jacoby⁵ has shewn that

¹ Poore, G. V. *Nervous Affections of the Hand and Other Studies*, p. 155, 1897.

² Rosenfeld. *Verhandl. d. deutsch. path. Gesellsch.*, 1904, vi, 71.

³ Eppinger. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1903, xxxiii, 123.

⁴ Wakeman, A. J. *Journ. Exper. Med.*, N.Y., 1905, vii, 303.

⁵ Jacoby. *Beitr. z. chem. Physiol. u. Path.*, Braunschweig, 1903, iii, 446.

the autolytic power of the liver is increased in phosphorus poisoning, and according to Wells¹ phosphorus destroys the liver cells but not their autolytic enzymes. The destruction of the liver cells causes hepatic inadequacy and so toxæmia, poisons which should have been arrested in the liver passing into the general circulation. It is thought that there is an acid intoxication due to sarcolactic acid in the blood.

Clinical Manifestations.—The symptoms due to the irritating effect of phosphorus on the gastric mucous membrane come on a few minutes to three hours after taking the poison. With phosphorated oil or phosphorus in a soluble state the effects appear rapidly, while if the poison was taken in a solid form, the onset is delayed. There is gastric pain, followed by vomiting, which greatly interferes with antidotal treatment and feeding, and may be so constant as to cause dangerous collapse. The vomited matters and eructations may be luminous in the dark, and dark and grumous from the presence of blood. There are usually intense thirst and tenderness over the stomach and liver, but no hepatic enlargement. The patient may die from collapse; if this does not occur and efficient treatment is carried out, permanent recovery may follow; but in a considerable number of cases there is a temporary improvement succeeded by the return of grave symptoms due to the effects of the absorbed poison on the liver and other internal organs. These severe symptoms usually begin about four days after the poison was taken; they may arise sooner, or, on the other hand, be delayed for two, three, or even six weeks (S. West²).

The scene reopens with jaundice and recurrence of grumous vomiting, followed by great prostration, coma, and death, usually on the fifth or sixth day from the time the phosphorus was taken, and after a day or two of grave constitutional symptoms. Haemorrhages into the skin and from mucous surfaces are constant and generally larger than in acute yellow atrophy. In one case there were extensive haemorrhages behind the peritoneum, which may have accounted for abdominal pain (Hann and Veale³). Jaundice is not always present, and does not bear any relation to the severity of the changes in the liver. The temperature is usually below normal. The liver is enlarged and tender; the spleen is also enlarged, and the abdomen may be distended. The most marked difference between this stage of phosphorus poisoning and acute yellow atrophy is in the size of the liver. But in exceptional cases the liver is not enlarged, and in the early stages of acute yellow atrophy it may be enlarged, so that the clinical resemblance between the two affections is sometimes very close.

In the early stages the number of red blood-corpuscles is often increased (v. Jaksch⁴); this is not necessarily due to concentration of the blood from vomiting, for it may occur in cases without vomiting.

¹ Wells. *Chemical Pathology*, p. 98, 1907.

² West, S. *Lancet*, Lond., 1893, i, 245.

³ Hann and Veale. *Lancet*, Lond., 1910, i, 163.

⁴ v. Jaksch. *Deutsche med. Wchnschr.*, 1893, xix, 10.



Occasionally there is a leucocytosis. The blood may become non-coagulable from absence of fibrinogen (Jacoby¹); its alkalinity is reduced, and it contains an excess of fat.

The urine is somewhat diminished in quantity, but never suppressed; it is high coloured and of rather high specific gravity. It may contain albumin, blood, casts, and albumose. Bile pigments and bile acids are generally present. It was formerly said that leucine and tyrosine are absent, and stress was laid on this as diagnostic from acute yellow atrophy; but it is now known that leucine and tyrosine may be present in the urine in phosphorus poisoning. Leucine is less frequently present than tyrosine. Arginine, alanine, and glycocoll have been found in the urine (Wohlgemuth²). The presence of leucine and tyrosine in the urine is due, like the albumosuria, to autolytic changes in the liver cells. That it is not, as was formerly thought, due to failure on the part of the liver to transform leucine and tyrosine into urea is shown by the fact that the experimental exclusion from the circulation of the liver in geese by ligation of the portal vein and hepatic artery does not lead to the appearance of leucine and tyrosine in the urine. The total nitrogen in the urine is increased after the first few days from excessive protein disintegration. Experimentally the rise in the protein metabolism in phosphorus poisoning is only equalled by that in phloridzin diabetes. In the second stage the percentage of urea in the total urinary nitrogen falls from the normal 90 to 70 or 80, and that of ammonia rises from the normal 4-6 to 10-18 per cent. The increased amount of ammonia in the urine can be diminished by the administration of sodium bicarbonate. The explanation of this is that, owing to an increase in organic acids in the body, ammonia is utilised as a base and appears in the urine in combination with organic acids; when sodium bicarbonate is given, the ammonia is no longer utilised in this way, and can therefore be converted into urea.³ In other words, the presence of ammonia in the urine, though associated with changes in the liver, is not due to any failure in the hepatic cells to form urea out of ammonia, but is evidence of incipient acid intoxication. Acetone, diacetic and sarcolactic acids are frequently present in the urine. Glycosuria is very rare; in 141 cases at Prag it was found in 6 (Walko⁴).

In 19 cases of phosphorus poisoning Frerichs⁵ gave large quantities (200 grams) of sugar, but obtained alimentary glycosuria in two only.

Diagnosis.—The history that phosphorus has been swallowed or that symptoms justifying this conclusion have recently occurred is a most important, if not an essential, point. The presence of phosphorus in the vomit or the luminosity of the vomited matters in the dark settles the question. In the diagnosis from acute yellow atrophy the large size

¹ Jacoby. *Ztschr. f. physiol. Chem.*, Strassburg, 1900, xxx, 175.

² Wohlgemuth. *Ibid.*, 1905, xlv, 74.

³ Vide Herter. *Lectures on Chemical Pathology*, p. 347, 1902.

⁴ Walko. *Ztschr. f. Heilk.*, 1901, ii, 339.

⁵ Frerichs, F. T. *Ueber den Diabetes*, 1884. Quoted by Williamson, *Diabetes*, p. 116.

of the liver and the greater prominence of gastro-intestinal symptoms should also be borne in mind. In the absence of a reliable history great difficulty may arise in the differential diagnosis; in fact, Poore¹ considered that clinically and pathologically the two conditions are indistinguishable.

Rapid cirrhosis with a greatly enlarged liver and cholaemia, and sporadic cases of Weil's disease may simulate phosphorus poisoning in the absence of a distinct history.

Prognosis.—In cases with jaundice and enlargement of the liver the outlook is very grave; most cases die.

Treatment.—When the poison has been recently taken, the stomach should be emptied and washed out with warm water containing sulphate of copper or 0·5 to 1 per cent solution of permanganate of potassium. As an antidote, old French or oxidised oil of turpentine should be given every quarter of an hour for the first hour, 40 minims in an emulsion, and afterwards three or four times daily. Mucilaginous drinks should be given, but oils and fats should be avoided, as they render the phosphorus more soluble. Purgatives are advisable. When the grave constitutional symptoms have developed, no special treatment can be relied on. But it would be reasonable to give large doses of sodium bicarbonate by the mouth or by subcutaneous transfusion to counteract acidosis. Enemas of dextrose 5 to 10 per cent may also be given.

INFECTIOUS JAUNDICE

AMONG the various forms of toxæmic or hæmo-hepatogenous jaundice there is a group which, in contradistinction to the malignant forms of toxæmic jaundice or icterus gravis, such as acute atrophy and phosphorus poisoning, is spoken of as benign infectious jaundice or merely infectious jaundice. Of this group, Weil's disease is a well-marked example. The general characters of toxæmic jaundice have already been sketched (*vide* p. 536), and it was there pointed out that the jaundice is subordinate both in degree and in importance to the constitutional symptoms of a general hæmic infection or intoxication. In many instances the primary infection constitutes a definite disease, as in the specific fevers, yellow fever, pyæmia, and septicaemia, but in this group of infectious jaundice, although there is a general disorder, its characters are not sufficiently typical to allow of its recognition as a definite disease apart from the febrile condition and jaundice.

There are thus many examples of toxæmic jaundice of undetermined nature grouped under the heading of infectious jaundice. The more severe cases are considered in a special category under the name of Weil's disease. Among the slight forms are some cases often termed catarrhal jaundice, but presenting fever and enlargement of the liver and

¹ Poore, G. V. *Nervous Affections of the Hand and Other Studies*, p. 155, 1897.





spleen; the onset of these cases is the same as that of catarrhal jaundice, but there are the above-mentioned additional features, which shew that there is not a mere local obstruction at the lower end of the bile-duct, but a more widespread infection. No doubt transitional cases between a local infection and obstruction at the lower end of the bile-duct and a more extensive obstruction of the ducts exist, and it is, therefore, convenient to speak of the cases as infectious catarrhal jaundice. It is not infrequent for epidemics of this form of jaundice to occur, and it is not always easy to be certain whether it is a mild infectious jaundice, the infection falling chiefly on the bile-ducts, or whether there is an epidemic form of gastro-intestinal catarrh in which the lower end of the bile-duct is obstructed, while the ducts remain free from more extensive infection.

The epidemic jaundice which occurred in our troops in the South African war (1899–1902) was regarded by some as infectious and by others as due to gastro-intestinal catarrh.¹

WEIL'S DISEASE

Synonyms: Infective Jaundice; "Bilious Typhoid."

IN 1886 Weil² described febrile jaundice associated with nephritis and enlargement of the spleen. It occurs in epidemics, one of which had previously been described by Weiss in 1866 as "infective jaundice." The disease was called after Weil, of Heidelberg, by his compatriots, but the French school did not consider that it differed from icterus gravis or infectious jaundice.

Weil's disease is an excellent example of acute infective jaundice due ^{to a haemae} ~~to~~ infection of the body by a ~~proteus bacillus~~. The jaundice is toxæmic, and has analogies with that induced experimentally by toluylendiamine. Some cases recorded as examples of recovery from acute yellow atrophy may have been examples of Weil's disease. Conversely, fatal cases of Weil's disease are sometimes described as acute yellow atrophy or icterus gravis.

Etiology.—It usually attacks young adults; some estimates give a percentage of 90 in males; it has been very rarely recognised in children.

Brüning³ reported a case, confirmed bacteriologically, in an infant 4 months of age.

The infection is probably due to eating decomposed meat or drinking water which has been infected by tainted meat or by the bodies of animals dying from a similar disease. Its frequency in the German army has been referred to the consumption of rancid and improperly

¹ Vide *Report of the Imperial Yeomanry Hospitals in South Africa*, 1902, iii, 195.

² Weil. *Deutsches Arch. f. klin. Med.*, 1886, xxxix, 209.

³ Brüning. *Deutsche med. Wchnschr.*, 1904, xxx, 1269.

cooked sausages (H. Brooks¹). Semmola and Geoffredi² quote cases apparently due to inhalation of sewer-gas. It is, therefore, more likely to occur in butchers, soldiers, and sewer-men. Most of the cases occur in the summer and in epidemics. It may arise repeatedly in the same place, ~~but does not appear to be contagious.~~

The disease is rare in England, though some epidemics of catarrhal jaundice have been erroneously described as Weil's disease, and is usually seen in Germany, Russia, and France. Few cases have been recorded in America (Raymond,³ Lamphear, H. Brooks, Libman,⁴ Satterlee,⁵ Einhorn). In Smyrna it has been endemic since 1837 and in Alexandria since 1870; Greeks appear to be specially susceptible (Sandwith⁶).

Bacteriology.—Jaeger,⁷ Banti,⁸ and others described a proteus bacillus as the essential cause. Jaeger found the same organism (*Bacillus proteus fluorescens*) in ducks dying with jaundice, which frequented the water in which his patients had bathed and presumably become infected. Satterlee tabulated the characters of the bacilli found by Weil, Jaeger, Brooks, Libman, and himself. This bacillus is found in the viscera in large numbers, and when cultivated and injected into animals, leads to acute degenerative changes in the liver and kidneys. It appears that bacilli are rarely present in the blood, and that dissemination occurs chiefly by the lymphatics (H. Brooks).

Morbid Anatomy.—The tissues of the body are bile-stained and shew the effect of a general toxic process. The liver is either somewhat increased in size, or of the normal volume. Haemorrhages may be present in the skin and in the mucous and serous membranes. The spleen is swollen, enlarged, and has been seen to contain haemorrhages. The kidneys shew tubal nephritis. There is cloudy swelling of the cells of the kidney, liver, and heart muscle, going on to the further degenerative change of fatty metamorphosis. The changes in the liver may progress further and resemble those in acute yellow atrophy; the mucous membrane of the bile-ducts becomes swollen and degenerated.

Symptoms.—The onset is sudden, and resembles that of influenza. The chief symptoms are malaise, headache, fever, rigors, severe muscular pains, especially in the calves, and often gastro-intestinal disturbance. The pulse-rate is about 120 at first, but becomes slower after the appearance of jaundice. Jaundice appears between the third and fifth days of the illness. In a case under my observation it did not appear until the seventh day. It is generally slight, and lasts about two weeks; the motions may be clay-coloured, but usually contain bile and are often

¹ Brooks, H. *Arch. Neurol. and Psychopath.*, N.Y., 1900, iii, 344.

² Semmola and Geoffredi. *Twentieth Century Practice*, 1897, ix, 688.

³ Raymond. *Med. Age*, Detroit, 1892. Quoted by Brooks.

⁴ Libman. *Phila. Med. Journ.*, 1899, iii, 620.

⁵ Satterlee. *Med. News*, N.Y., 1903, lxxxii, 1069.

⁶ Sandwith. *Brit. Med. Journ.*, 1904, ii, 672.

⁷ Jaeger. *Ztschr. f. Hyg.*, 1892, xii, 525.

⁸ Banti. *Deutsche med. Wchnschr.*, 1895, xxi, 493.

Spirochaeta Jarrovi ^[Swine] ^{Linton, Gulland and}
 Cases in this country have been reported by Ryle, Manson-Bahr, ^{G.} Buchanan ^{'East}
 In East Indian mines rats were found to be infected and out of
 13 miners attacked 4 died.

In Japan a disease with similar clinical features has been
 shown to be due to the *Spirochaeta icterohaemorrhagica* which
 disappears from the blood after the 7th day. It is found in the liver
 cells and in larger numbers ^{in the} kidneys. The spirochaete which is
 excreted by the urine is thought to gain entrance to the body through
 the skin, though mainly by the alimentary canal. The presence of the
 spirochaete was ^{subsequently} ~~also~~ found in the blood during the early days of the
 disease during the great European war.

Ryle
 Manson-Bahr Lanat, 1922, ii, 1056
 Gulland and Buchanan, Brit. Ind. Journ., 1924, i, 313

JNADA, IDO, HOKI, KANEKO, and ITO Journ. Exper. Med., N.Y., 1916, XXIII, 377



loose. The liver becomes enlarged and tender. A marked feature of the disease is the splenic enlargement. Fever reaching 103° to 104° F. lasts for about a week; the temperature then falls and becomes normal at about the tenth day.

Max Einhorn¹ has recorded two cases in which small tumours were temporarily palpable on the surface of the liver.

Nervous symptoms are prominent; the muscular pains in the calves are severe, prostration, giddiness and stupor may be marked, so that

the patient appears gravely ill, and delirium is usually present. Epistaxis, purpura, and rashes, such as herpes, erythema, and urticaria, may be met with. A relapse may occur a week or so after the temperature has become normal; its occurrence may be suspected if, after the first attack, the spleen remains enlarged. The relapse lasts about a week. Chauffard² describes Weil's disease as "relapsing infectious jaundice," but in Germany relapses are comparatively infrequently described; thus, in 84 cases, of which 73

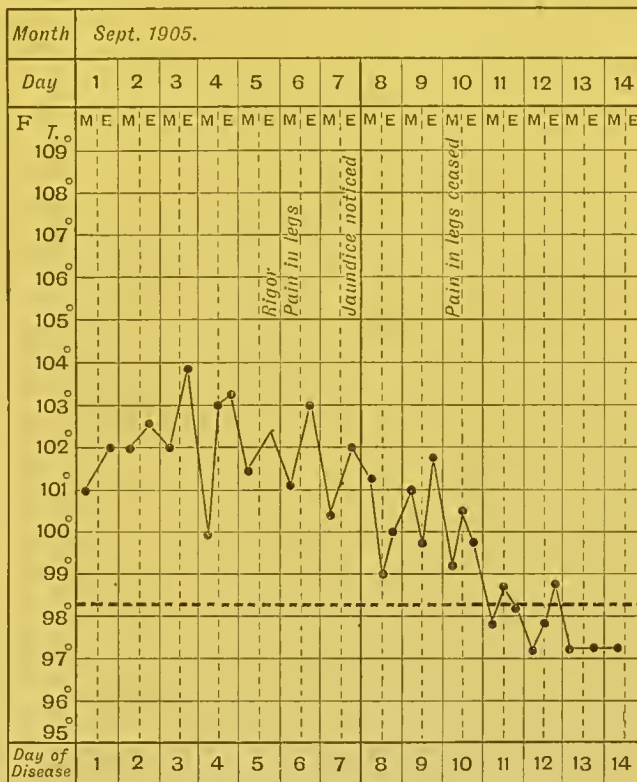


FIG. 81.—Chart of a case of Weil's disease.

were collected from German literature, Tymowske³ found relapses mentioned in 19. Quinke⁴ says that a relapse occurs in 40 per cent of the cases.

The blood is ~~almost always~~ sterile, and the proteus bacillus, described by Jaeger and others, in the viscera, is not to be found in the general circulation. In some cases the blood-serum agglutinates the *Bacillus typhosus* even when diluted (Eckhardt⁵).

¹ Max Einhorn. *Am. Journ. Med. Sc.*, Phila., 1904, cxxviii, 896.

² Chauffard. *Traité de médecine* (Bouchard, Brissand), v, 98.

³ *Thèse de Paris*, 1889, quoted by Chauffard, *loc. cit.*

⁴ Quinke. "Diseases of the Liver," in Notnagel's *Encyclopedia of Practical Medicine*, English translation, p. 504, 1903.

⁵ Eckhardt. *München. med. Wchnschr.*, 1902, xlix, 1129.

The urine is scanty, albuminous, contains bile-pigment, casts, and sometimes blood-corpuscles and bile acids. ~~It shows the proteus bacillus found in the viscera. Bacteriuria may persist for a considerable time; in Satterlee's case, in which it was still present and rendered the urine turbid a month after the disease, it may have been due to local infection of the prostate.~~

Diagnosis.—Fever, jaundice, enlarged spleen and liver, pains in the calves, and albuminuria occurring in epidemics, running an acute course, and ending in recovery are the characteristics of the special form of infectious jaundice called Weil's disease. Very similar forms of infectious jaundice occur and differ in some clinical features, such as the absence of albuminuria or constant association with gastro-intestinal symptoms. It is, indeed, hardly worth while to separate Weil's disease from these forms of infectious jaundice.

From ordinary *catarrhal jaundice* it is distinguished by its greater severity and by evidence of its being not a local disease limited to the bile-ducts, but a general infection, as shewn by albuminuria and bacteriuria.

From Enteric Fever.—Griesinger originally described the disease as "bilious typhoid." Not uncommonly cases of Weil's disease occur in association with typhoid fever. Further, according to Eckhardt, the blood-serum in Weil's disease may agglutinate typhoid bacilli even when diluted. It has been suggested that Weil's disease is modified typhoid fever, or typhoid infection limited to the biliary tract. The onset of Weil's disease is sudden, and gradual in enteric fever. The duration and course of Weil's disease are shorter than those of enteric fever, in which jaundice is extremely rare.

The more severe examples of Weil's disease approach icterus gravis and acute yellow atrophy. Relapsing fever should be recognised by detection of the *Spirillum obermeieri* in the blood. Dengue and mild yellow fever resemble Weil's disease, but the diagnosis can usually be made from consideration of the surroundings.

The **prognosis** is fairly favourable in Europe, but convalescence may be protracted. ~~The mortality varies considerably in different parts of the world~~

In the 44 cases obtained by adding Weil's, Jaeger's, Haas's, and Wassilieff's figures there were only five deaths. In 300 cases at the Greek Hospital in Alexandria the average mortality was 30 per cent, but at different times it varied from 10 to 60 per cent (Sandwith).

Treatment.—The patient should remain in bed until after the temperature has become normal, and should be restricted to a milk diet. All alcoholic drinks should be interdicted, and the patient should be encouraged to drink freely of water. Intestinal antiseptics, such as ealomel ($\frac{1}{20}$ gr.) in minute doses, salol, salicylate of bismuth, or β -naphthol, should be given. Copious enemas of water have been recommended. ~~The treatment is on the same lines as that of catarrhal jaundice (vide p. 869).~~

The Spirochaeta icterohaemorrhagica appears in the urine at an early stage and diminishes in numbers to disappear before the 40th day.

In Japan the mortality is estimated at 32 per cent.

The intravenous injection of convalescents and of Salvarsan and the serum of goats and horses immunized with Spirochaeta icterohaemorrhagica have both given good results, when employed early in the course of the disease. (INADA, IDO, ITO, HOKI, & WANI.)

INADA, IDO, HOKI, ITO, & WANI. CONV. f. SCHWEIZ. AERZE, Basel, 1917, XLVII, 65

Both experimentally and in man.
 Thomas finds that destruction or loss
 of function of the gall bladder often leads
 to dilatation of the extrahepatic ducts,
 but that the dilatation does not exert
 any harmful influence. Martin records
 a case in a child one year old without any
 dilatation of the common duct.

In Stone's case the common
 bile and hepatic ducts
 contained calculi

Thomas. Boston Med. and Surg. Journ., 1920
 CLXXXIII, 282
 Martin, W. Ann Surg., 1924, LXXIX, 444.
 Stone. Am. Journ. Med. Sc., Phila., 1908
 CXXXV, 889
 Seigchnor, A. Maryland Med. Journ., Baltimore
 1917, LX, 211

DISEASES OF THE GALL-BLADDER

ABNORMALITIES.—Absence of the gall-bladder is the normal condition in the horse, mule, ass, elephant, and other animals. It is sometimes seen in man, and Gay¹ has collected 19 cases; but some of the older observations, such as those of Cholmeley² and Thomas,³ were evidently cases of obliteration of the gall-bladder due to inflammation during fetal life. I have seen one case at St. George's Hospital in a man aged forty-nine who died from pulmonary tuberculosis (Latham⁴). Congenital absence of the gall-bladder has been associated with imperfect development of the pancreas and imperforate anus (Blakeway⁵). In genuine cases the common bile-duct is sometimes dilated in part of its course. The change has also been described after ~~removal of the gall bladder~~ (Mayo Robson⁶). A) rate,

Crucknell's⁷ case, in which the common hepatic duct was described as opening into the gall-bladder and the common bile-duct as coming off separately from the gall-bladder, so that all the bile must have passed through the "gall-bladder," was probably a case of absence of the gall-bladder with compensatory dilatation and pouching of the upper end of the common bile-duct. A

Two gall-bladders, each with a cystic duct, have been recorded in exceptional instances.

Purser⁸ described an example in 1886 and referred to a case recorded in the Philosophical Transactions of 1693-4 in which there was a gall-bladder on the left lobe and another on the right lobe of the liver. Sherren⁹ removed two gall-bladders placed side by side, each with a cystic duct, from a woman aged twenty-five. *Other cases have been reported by Seachner*

Bifid Gall-bladder.—A longitudinal septum has been known to divide

¹ Gay. *Trans. Chicago Path. Soc.*, 1902, v, 108.

² Cholmeley. *Med. Trans. Roy. Coll. Phys.*, Lond., 1820, vi, 50.

³ Thomas. *Med. Times*, 1848, xvii, 171.

⁴ Latham. *Journ. Anat. and Physiol.*, 1898, xxxii; *Proc. Anat. Soc.*, p. xxxix.

⁵ Blakeway. *Lancet*, Lond., 1912, ii, 365.

⁶ ~~Mayo Robson. *Brit. Med. Journ.*, 1906, i, 431.~~

⁷ Crucknell. *Trans. Path. Soc.*, Lond., 1871, xxii, 163.

⁸ Purser. *Brit. Med. Journ.*, 1886, ii, 1106.

⁹ Sherren. *Ann. Surg.*, 1911, liv, 204.

the gall-bladder into two halves. A specimen (No. 1014) from King's College Hospital Museum is figured by Moynihan.¹ ^

Malposition.—In rare instances the gall-bladder is found to the left of the longitudinal fissure and on the under surface of the left lobe.

There is a specimen in the Anatomical Museum, Cambridge. Duvé² figures a case, and Walton³ records it in a full-time female child. *Shelton & Child*
13000

In cases in which the left lobe is atrophied the gall-bladder appears to be attached to the left margin of the liver (*vide* Fig. 3), and may have its long axis at a right angle to that of the body.

In some instances the fundus of the gall-bladder is embedded in the substance of the liver, and may shew through on the anterior surface like a cyst in the substance of the right lobe. The notch at the anterior margin of the liver is absent in these cases. In exceptional instances the posterior surface of the gall-bladder may be covered over for some distance by a bridge of liver substance and justifies the term intra-hepatic gall-bladder (Duvé, Loughran,⁴ Wieder⁵). A gall-bladder so situated would probably not contract so well as a healthy one, and would thus be disposed to infection and cholelithiasis. Lemon⁶ recorded a gall-stone in an intrahepatic gall-bladder. Not very rarely there is a kind of mesentery to the gall-bladder so that it is unusually movable. Brewer⁷ found that in 5 out of 100 bodies this mesentery was the only attachment of the gall-bladder to the liver. This would favour the occurrence of torsion of the gall-bladder, a very rare event; Nehr-korn⁸ and Wendel⁹ have recorded gangrene, and Lett,¹⁰ strangulation of the gall-bladder due to torsion.

The gall-bladder has been found in the sac of a femoral hernia.¹¹

Abnormalities in Size and Shape of the Gall-bladder.—Quite apart from inflammation or gall-stones the fundus of the gall-bladder, just where it projects beyond the anterior margin of the liver, may shew a constriction which resembles the pathological hour-glass gall-bladder. The projecting portion of the gall-bladder may be twisted like a fish-hook (Duvé). In rare instances fat is found under the peritoneal coat of the gall-bladder; it is of no pathological importance. Subserous oedema is sometimes present in cases of ascites, in the backward pressure of heart-disease, and occasionally when there is no associated pathological change.

¹ Moynihan. *Gall-stones and their Surgical Treatment*, p. 37. 1906.

² Duvé. *Bull. Soc. Anat.*, Paris, 1903, lxxviii, 261.

³ Walton. *Lancet*, Lond., 1912, i, 925.

⁴ Loughran. *Ibid.*, 1905, ii, 483.

⁵ Wieder. *Univ. Penna. Med. Bull.*, Phila., 1905, xviii, 213.

⁶ Lemon. *Lancet*, Lond., 1905, i, 1265.

⁷ Brewer. *Ann. Surg.*, 1899, xxix, 721.

⁸ Nehr-korn. *Deutsche Ztschr. f. Chir.*, Leipz., 1908, xevi, 319.

⁹ Wendel. *Ann. Surg.*, 1898, xxviii, 199.

¹⁰ Lett. *Lancet*, Lond., 1909, i, 1099.

¹¹ Battle, *Trans. Clin. Soc.*, Lond., 1904, xxxvii, 245; Waring, *Diseases of the Liver*, 235, 1897.

- the cysto-duodenal or cysto-jejunal -

A peritoneal fold may pass from the gall-bladder to the duodenum or over the transverse colon into the great omentum; it is an abnormality not a pathological change (FLINT). It may lead to kinking of the cystic duct and closely imitate a calculus in that situation (Gray and Anderson).

^) of which Frankau refers to 11, ^{and Daux to 17} recorded examples

FLINT. Bull. Johns Hopkins Hosp., Balt., 1912, XXIII, 302.

Gray and Anderson. Lancet, London, 1913, I, 1300.

Schachner. Ann Surg., 1916, LXN, 419

Frankau, C. Brit. Journ. Surg., Bristol, 1922, X, 301

Daux, F. Thèse de Paris, 1924 or 5

Torsion or Volvulus of the Gall-bladder

This is a rare condition, of which Frankau collected 11, and Daux 17 examples. There are two forms (1) of the whole gall-bladder and (2) more exceptionally of the fundus only. It is dependent on one of two congenital abnormalities, the presence of a mesentery as the peritoneal attachment of the gall bladder to the liver, or the absence of such an attachment so that the gall bladder hangs free in the abdominal cavity. Contrary to what might therefore be anticipated eight of the 17 ^{Daux's} cases occurred between the ages of 70 and 79 years. ^{Sixteen out of the 17} cases were in females. ^{out of 9 cases mentioned by Jonas (these were calculated in 2.)} The clinical picture is that of the acute abdomen. In 2 cases gangrene occurred.

The treatment is cholecystectomy. But of the 17 cases 5 (one of whom was ^{not} operated upon) proved fatal.

Frankau

Daux

Jonas, H.C. Brit Med. Journ., 1923, 1, 1016.

ACUTE CHOLECYSTITIS

ACUTE CHOLECYSTITIS has various degrees of intensity ; it may, like appendicitis, be catarrhal, suppurative, ulcerative, phlegmonous or gangrenous, according to the virulence of the infection and the resistance of the organ. Inflammation which at first is sero-fibrinous may subsequently become purulent, so that what is an acute serous cholecystitis at the outset may eventually present itself as an empyema of the gall-bladder. The causes of acute cholecystitis will first be considered generally, and then a separate description will be given of the acute catarrhal, suppurative, phlegmonous, and gangrenous forms.

Causes.—Acute inflammation of the gall-bladder is very closely bound up with the same process in the ducts, and from the point of view of causation it is rather an artificial distinction to describe these two conditions separately. Acute inflammation may begin in the ducts, as in suppurative cholangitis due to the rupture of an hydatid cyst into the ducts, and spread to the gall-bladder. In some instances an acute cholangitis may infect the gall-bladder, which eventually goes on to suppuration while the primary lesion resolves. On the other hand, acute inflammation may begin in the gall-bladder, as in typhoidal infection, and remain limited to it, or subsequently spread to the ducts. The conditions leading to acute cholecystitis, whether suppurative or not, are : (1) *Disposing* ; (2) *exciting*.

I. Disposing Causes.—The factors which reduce the resistance of the gall-bladder and render it more liable to infection and inflammation are : (a) A previous attack of inflammation of the gall-bladder. Micro-organisms may remain in a latent condition, as in “typhoid carriers,” and a relapse may be induced. Further, mild cholecystitis may lead to the formation of calculi.

(b) Calculi in the gall-bladder ~~may, by their action,~~ render infection more easy.

(c) The rare occurrence of foreign bodies, such as worms or the ova of parasites, in the gall-bladder would have a similar influence to calculi in the gall-bladder.

(d) Factors causing biliary obstruction favour the multiplication of any micro-organisms which have gained entrance to the gall-bladder, inasmuch as they are not flushed out, but remain in that viscus. These factors are discussed under the heading of Gall-stones (p. 713), and include sedentary habits, obesity, abdominal tumours, pregnancy, tight lacing, and other conditions which interfere with the descent of the diaphragm.

II. Direct or Exciting Causes.—(a) Infection of the gall-bladder ; this is the cause of almost all the cases. (b) Toxins reaching the gall bladder and, in the absence of any micro-organisms, setting up cholecystitis. This is largely theoretical. (c) Trauma of the gall-bladder.

(A) Infection.—The infectious diseases which lead to local manifestations in the gall-bladder may be divided into two classes, which, however, to a certain extent, overlap: (1) Haemic infections. (2) Diseases of the alimentary canal.

(1) *In haemic infections*, such as pyaemia and septicaemia, micro-organisms may reach the gall-bladder, ~~being excreted into its cavity and into the bile-ducts from the branches of the hepatic artery.~~ Acute cholecystitis may follow pneumonia and be due to pneumococcal infection. In chronic Bright's disease terminal infections are not uncommon and may involve the gall-bladder. Acute cholecystitis apparently following influenza, but resolving, so that no proof of its nature can be obtained, is probably not very rare. Some of the cases of jaundice following influenza may shew cholecystitis, as well as inflammation of the ducts.

F. A. Packard¹ records a case of influenzal cholecystitis. A man aged forty was admitted under my care with the pains of influenza. He had had a sudden onset of vomiting and intense colic, like that of gall-stones. There was tenderness over the gall-bladder, which could not be felt, and the vermiform appendix, but there was no jaundice and no calculus could be found in the stools. He made a rapid recovery. The case appeared to be one of the gastro-intestinal form of influenza with cholecystitis.

(2) *In diseases of the alimentary canal* infection of the gall-bladder is due to the passage of micro-organisms, especially the colon and typhoid bacilli, from the bowel to the gall-bladder. Infection of the gall-bladder might be due to direct extension up the common bile-duct. In the case of typhoidal cholecystitis there are grounds for doubting this (*vide* p. 607). Under normal conditions the empty duodenum is sterile, or almost so; it is probable that in the absence of duodenal inflammation micro-organisms reach the gall-bladder by the portal vein rather than by direct extension up the common bile and cystic ducts. Influenza, in virtue of its gastro-intestinal form, comes into this group. The relations of appendicitis and cholecystitis with or without gall-stones are interesting. The two conditions may coexist (*vide* also p. 716); this has been frequently noticed in operations (Moynihan²). Evidence of this in routine post-mortem work is not striking: among 841 consecutive necropsies at St. George's Hospital Mr. Frankau found 50 cases of cholelithiasis or cholecystitis; in two of these, or 4 per cent, there was appendicitis. ~~It is possibly that~~ in some cases both organs are attacked by a simultaneous infection; that in others appendicitis is primary and provides an inlet for micro-organisms which set up cholecystitis (Ochsner,³ Sheldon⁴), or, lastly, that the cholecystitis is primary and the appendicitis secondary (Dieulafoy⁵). Cholera (Gal-

¹ Packard. *Phila. Med. Journ.*, 1899, iv, 879.

² Moynihan. *Lancet*, Lond., 1912, i, 9.

³ Ochsner. *Phila. Med. Journ.*, 1900, vi, 652.

⁴ Sheldon. *Journ. Am. Med. Assoc.*, Chicago, 1906, xlviii, 1458.

⁵ Dieulafoy. *Pressc méd.*, Paris, 1903, p. 445.

and, Caplesco arguing that the appendicitis though
primary is often clinically latent.

Caplesco, C.P. Bull. Acad. Méd., Paris, 1924, 2^e s^ér., XCII, 869
J. S.

Cholecystitis due to infection with hemolytic
Streptococci, derived from the teeth and
tonsils and having a special affinity for
the gall bladder, has been especially
investigated by Rosenow and Brown, who
argue that B. Coli formerly regarded as
one of the two most important micro-organisms
in the causation of cholecystitis is often a
secondary invader

Rosenow Journ Amer. Med. Assoc., 1914, LVIII, 958
Surg., Gyn. & Obst., 1921, XXXIII, 19
Brown. Arch. Int. Med., Chicago, 1919, XXIII, 185.

Thomas New York Med. Journ.,
1907, LXXXII, 608

liard¹), oral sepsis (Daniel²), and intestinal kinks (Lane³) have been thought to cause cholecystitis.

Cholecystitis due to Infection with Bacillus Coli.—This subject is of great importance in connexion with the production of gall-stones, and is referred to under that heading. Colon bacilli probably reach the gall-bladder mainly by the portal vein, but an ascending infection from the biliary papilla may occur when there is duodenitis. Infection of the gall-bladder may follow intestinal disorders in which the colon bacilli become virulent, or may be due to absorption of bacilli from an intestinal ulcer or an inflamed vermiform appendix.

Cholecystitis due to Typhoidal Infection.—That inflammation of the gall-bladder may complicate typhoid fever has been known since Louis' and Andral's time (1829). Budd,⁴ Ayres,⁵ and Pepper⁶ recorded early cases. For good résumés of the history of typhoidal cholecystitis see A. L. Mason's⁷ and Camac's⁸ articles. Gilbert and Girode,⁹ in 1890, first proved bacteriologically that suppurative cholecystitis may be due to typhoid bacilli. Numerous cases confirming this discovery have since been reported by Chiari¹⁰ and others.

Cholecystitis during or after typhoid fever is not always due to infection with *Bacillus typhosus*. Thus, Cushing¹¹ met with 5 cases of post-typhoidal cholecystitis in which a pure culture of *B. coli* was obtained. There may be a mixed infection of *B. coli* and *B. typhosus*, as in Marsden's¹² case.

The incidence of cholecystitis in enteric fever is difficult to estimate, inasmuch as the slighter cases often escape detection. Sometimes palpation of the gall-bladder causes pain, but as there are no further symptoms it is impossible to speak with certainty as to the condition of affairs. Murchison¹³ and Kelly's¹⁴ observations are in favour of latent cholecystitis in enteric not being uncommon. It probably occurs clinically in less than 1 per cent of the cases. Camac collected

Thomas

184 ~~45~~ cases with infection in 30

In 620 cases of enteric at Montreal tabulated by Stewart¹⁵ there were 7 examples of cholecystitis, of which 1 (suppurative) was fatal. In 1016 cases of enteric fever admitted into the Imperial Yeomanry Hospitals in South Africa

¹ Galliard. *La Choléra*, Bibliothèque Charcot-Debove, 1894.

² Daniel. *Brit. Med. Journ.*, 1910, i, 121.

³ Lane. *Ibid.*, 1912, i, 991.

⁴ Budd. *Diseases of the Liver*, p. 195, 2nd ed., 1852.

⁵ Ayres. *New York Journ. Med.*, 1846, vii, 315.

⁶ Pepper, W., Sr. *Am. Journ. Med. Sc.*, 1857, N.S., xxxiii, 13.

⁷ Mason, A. L. *Trans. Assoc. Am. Phys.*, 1897, xii, 23.

⁸ Camac. *Am. Journ. Med. Sc.*, 1899, cxvii, 275.

⁹ Gilbert et Girode. *Compt. rend. Soc. Biol.*, Paris, 1890, xlii, 756; *ibid.*, 1893, xlv, 956.

¹⁰ Chiari. *Ztschr. f. Heilk.*, 1894, xv, 199.

¹¹ Cushing. *Johns Hopkins Hosp. Bull.*, Balt., 1898, ix, 91.

¹² Marsden. *Med. Chron.*, Manchester, 1901, 3. s., iv, 269.

¹³ Murchison. *Continued Fevers*, p. 634, 3rd ed., 1884.

¹⁴ Kelly, A. O. J. *Am. Journ. Med. Sc.*, Phila., 1906, cxxxii, 446.

¹⁵ Stewart, J. *Brit. Med. Journ.*, 1901, i, 1465.

during the War 1900-1901, 1 case only of cholecystitis was sufficiently marked to require operation or to be recognised beyond any doubt. Among 2864 patients with enteric in Philadelphia there were 18 cases of cholecystitis, or 0.62 per cent (Ashhurst¹). Among 1500 cases of enteric fever at the Johns Hopkins Hospital there were 19 cases of cholecystitis, or 1.2 per cent (T. M'Crae²). In these 6000 cases there were 45, or 0.8 per cent, cases of cholecystitis.

Three children Typhoidal cholecystitis usually occurs in young adults, but cases in *girls* of five, six, and ten years old have been recorded (Alexieff,³ Mason,⁴ Armstrong⁵). There is very considerable variation in the interval between the attack of typhoid fever and the cholecystitis. It may complicate the attack or may occur as long as fourteen or twenty years after (Camae). In some instances there is no history of typhoid fever (Cushing,⁶ Richardson,⁷ Kelly⁸); so that there is primary typhoidal cholecystitis. Cholecystitis complicating typhoid fever is seldom associated with cholelithiasis; among Camae's 115 collected cases of typhoidal cholecystitis there were 4 with gall-stones. The presence of gall-stones would dispose the gall-bladder to inflammation should enteric fever supervene. Acute cholecystitis months or years after typhoid fever is more often associated with cholelithiasis. Typhoid "carriers" not uncommonly have gall-stones which no doubt favour persistence of the bacilli in the gall-bladder; a vicious circle thus results. *More typhoid* The typhoid bacilli may conceivably reach the gall-bladder by several *lymphatics* routes, viz. by the portal vein, the hepatic artery, the common bile-duct, or possibly even through the walls of the bowel.

By the Portal Vein.—The bacilli have but a short way to travel to reach the liver by the portal vein; here they set up focal necroses, and, having thus injured the liver tissue, are able to pass into the bile-ducts. Sherrington⁸ shewed that bacilli alone, even though teeming in the blood, cannot pass through normal hepatic tissues, but that some previous damage by their toxins is necessary. Carmichael⁹ also found that after injections of typhoid cultures into the portal vein the bile remains sterile. It is, however, not improbable that during typhoid fever the walls of the ducts or of the gall-bladder become damaged by toxins excreted from the blood-stream and so permeable to micro-organisms, and that typhoidal infection from the portal vein may then take place.

From the Hepatic Artery.—Typhoid bacilli are present in the general circulation during the incubation period and there is strong evidence that they pass directly from the circulation into the intrahepatic bile-ducts and so reach the gall-bladder, and may thus set up a descending cholecystitis. Doerr¹⁰ finds

¹ Ashhurst. *Am. Journ. Med. Sc.*, Phila., 1908, cxxxv, 541.

² M'Crae, T. *System of Medicine* (Osler and M'Crae), 1907, ii, 137.

³ Alexieff. Abstract in *Am. Journ. Med. Sc.*, 1897, cxiv, 466.

⁴ Mason. *Trans. Assoc. Am. Phys.*, 1897, xii, 23.

⁵ Armstrong. *Brit. Med. Journ.*, 1911, ii, 1298.

⁶ Cushing. *Bull. Johns Hopkins Hosp.*, Balt., 1898, ix, 92.

⁷ Richardson, M. *Am. Journ. Med. Sc.*, Phila., 1898, cxv, 648.

⁸ Sherrington. *Journ. Path. and Bacteriol.*, Lond., 1893, i, 258.

⁹ Carmichael. *Ibid.*, 1903, viii, 276.

¹⁰ Doerr. *Centralbl. f. Bakt.*, 1905, xxxix, 624 (Orig.).

1/ Lowenburg.

Reid and Montgomery believe 18 cases failed
or operated on under 15 yrs of age with
typhoid cholecystitis

1/ Dudgeon

The previous incidence of enteric fever in cases of cholecystitis and
gallstones. Conditions so often combined, has been estimated at from
19 (Chauffard) to 10 (McGuire) or even 5 percent (Blasland). ^{there was} Vide also p 71.
Among 888 cases of gall bladder disease Blacklock obtained a history of
enteric fever in 28 percent.

Lowenburg. Arch. Pediat., N.Y., 1913, xxx, 212.

Reid and Montgomery Bull. Johns Hopkins Hosp., Balt., 1920, xxxv, 7.

Dudgeon. Lancet, Lond., 1908, ii, 1651.

Chauffard Le mens. de l'Association Chir., 1914, p. 36

McGuire Surg., Gyn., & Obstet., 1920, xxxi, 517

Blasland Practitioner, ^{Lond.} 1914, xcii, 646.

Blacklock. Bull. Johns Hopkins Hosp., Baltimore, 1924, 35, 391.

Lymphatic extension from the liver
to the walls of the gall bladder is
according to E.A. Graham and
Peterson much more important
in the production of cholecystitis
than a descending infection of
micro-organisms passing into
the bile

The observations of J. Koch
and Chiarolanza show that
the typhoid bacilli reach the
walls of the gall bladder by
the hepatic artery; and
Rose now believes that micro-
organisms, especially streptococci
have a selective affinity for the
gall bladder, in which necrosis
of the mucosa follows capillary
embolism.
Meyer, Neilson and Feustel,
however, conclude that the
hemato-hepatogenous route is
the only one that has been proved
experimentally

A. and B.,

B. pyocyaneus,
B. influenza,
B. enteritidis of
Gaertner (DEAN),
the comma bacillus (Freig),

Koch, J. Ztschr. f. Hyg. ¹⁹⁰⁹ LXII, 1
Chiarolanza. Ibid. LXII, 11
Meyer, Neilson & Feustel. Journ. Infect. Dis.
Chicago, 1921, XXVIII,
465.

DEAN, G. Journ. Hyg., Cambridge, 1911, XI,
259.
GREIG. Lancet, Lond., 1912, II, 1423.

Peterson, Priest and E.A. Graham Arch. Surg., 1921, II, 92
Peterson, M.G. Surg., Gyn., and Obstet., 1923, XXXVI, 522

that experimental injection of typhoid bacilli into the systemic veins is followed by the presence of bacilli in the bile, and as ~~section~~ of the cystic duct prevents the appearance of bacilli in the gall-bladder, and ~~section~~ of the common bile-duct does not have this effect, Doerr concludes that the bacilli enter the bile in the liver. Δ

By Direct Extension up the Common Bile-duct.—The motile typhoid bacilli might readily travel from the duodenum up the common bile-duct and reach the gall-bladder. An ascending infection of the gall-bladder from the duodenum was formerly accepted. Cushing and Livingood,¹ however, in experiments on the bacteriology of the duodenum, find that it is often sterile when empty, while the lower portion of the small intestine contains numerous micro-organisms. ~~This would render an ascending infection of the ducts improbable. Again, if typhoidal cholecystitis were an ascending infection, other micro-organisms, such as the Bacillus coli or streptococci, would probably be present, and the pancreas should be as often affected as the bile-duct. On these grounds it is unlikely that the infection in typhoidal cholecystitis is an ascending one.~~

It has been suggested that micro-organisms pass directly through the walls of the intestine into the peritoneal cavity and then through the walls of the gall-bladder. This may take place when both the viscera concerned are inflamed and so allow of the passage of micro-organisms through their walls; in this way a secondary infection of the gall-bladder when already inflamed may be brought about, but it is highly improbable that the gall-bladder is primarily infected in this way. *Take in place from next page.*

The typhoid bacilli ~~are~~ probably ~~derived from the blood in the liver and pass down the ducts into the gall-bladder.~~ The gall-bladder constantly contains typhoid bacilli in fatal cases of typhoid fever, and commonly in pure culture; this contrasts with the comparative infrequency of cholecystitis. As shewn by Thiroloix and Debré's² experiments, some additional factor, such as trauma, previous disease, gall-stones, or extreme stagnation of bile, is necessary to enable the bacilli to set up cholecystitis.

Bacteriology of Cholecystitis.—Besides the colon and typhoid bacilli, paratyphoid bacilli, ~~(Cocci)~~ streptococci, staphylococci, pneumococci, Friedländer's pneumobacillus (Clairmont⁴), *Micrococcus melitensis* (Bull and Gram⁵), ~~may give rise to cholecystitis.~~ The *Diplococcus pneumoniae* may attack the gall-bladder primarily, there being no pulmonary or other manifest lesions. Pneumococcic cholecystitis is usually more acute and severe than that due to colon or typhoidal infection. Mignot⁶ found that there was no remarkable anatomical difference in experimental cholecystitis due to streptococci, staphylococci, or the colon bacillus. Secondary infections may occur, so that typhoid bacilli, streptococci, staphylococci, etc., may be found together. From operation cases of pyopneumocholecystitis Pende⁷ cultivated *Bacillus aerogenes capsulatus* as

reach the
gall-bladder
from the blood
stream

¹ Cushing and Livingood. *Johns Hopkins Hosp. Rep.*, Balt., 1900, ix, 543.

² Thiroloix et Debré. *Rev. de méd.*, Paris, 1903, xxviii, 401.

³ ~~Cocci.~~ *Arch. Int. Med.* Chicago, 1910, v, 610.

⁴ Clairmont, P. *Wien. klin. Wchnschr.*, 1899, xii, 1068.

⁵ Bull og Gram. *Norsk Mag. f. Laegevidensk.*, Christiania, 1911, lxxii, 1026.

⁶ Mignot. *Thèse de Paris*, 1897.

⁷ Pende. *Policlín.*, Roma, 1907, xiv, 540.

well as other organisms. In primary typhoidal cholecystitis the inflamed gall-bladder may become adherent to adjacent intestinal coils, and the tissues being inflamed, micro-organisms may pass from the bowel into the gall-bladder.

Wunschheim¹ records a case bearing this interpretation. In a fatal case of typhoid fever the gall-bladder contained pus and typhoid bacilli, while the peritoneal lymph on the surface of the gall-bladder shewed the *Staphylococcus pyogenes aureus*, which was regarded as a secondary infection from the intestine.

(B) **Toxic Cholecystitis.**—Although, practically speaking, acute cholecystitis is always due to bacterial infection of the gall-bladder, it has been shewn by Wakeman's² and Claude's³ experiments that chemical and bacterial poisons are capable of inducing changes allied to inflammation in the gall-bladder.

Wakeman injected strong solutions of perchloride of mercury, carbolic acid, and ricin into the gall-bladders of dogs under antiseptic precautions, and produced considerable epithelial proliferation and desquamation, congestion of the vessels of the submucosa, and thickening of the walls of the gall-bladder. The amount of cholesterin in the bile was increased, but no calculi were formed. In 82 animals poisoned with abrin or with the toxins of diphtheria, tetanus, streptococci, staphylococci, *Bacillus coli*, and *Bacillus pyocyaneus*, Claude found hæmorrhages into the gall-bladder in 7. \wedge

On the analogy of toluylenediamine, which sets up an inflammation of the small ducts in the liver which may spread down into the duodenum (Hunter⁴), it is reasonable to assume that toxic inflammation of the small bile-ducts in man might extend into the gall-bladder and set up acute cholecystitis. Such a toxic cholecystitis would probably soon become infected with micro-organisms from the blood-stream. As the matter stands, cholecystitis due to poisons, as apart from infection, is a theoretical possibility rather than an established occurrence in practice.

(C) **Trauma**, such as a fall or blow in the region of the gall-bladder, may so reduce its resistance that any micro-organisms present, which would otherwise be removed or destroyed, are enabled to set up inflammation. It is known, for example, that in typhoid fever the bacilli are always present in the gall-bladder, but that cholecystitis is comparatively infrequent. Trauma in such cases would be an exciting cause of cholecystitis. A blow may set up acute inflammation in cases in which a calculus is latent in the gall-bladder.

Kehr⁵ reports the case of a doctor, who after being knocked down by a bicyclist, rapidly developed acute inflammation in a contracted gall-bladder, the

¹ Wunschheim. *Prag. med. Wchenschr.*, 1898, xxxiii, 13.

² Wakeman. Quoted by Herter, *Med. News*, N.Y., 1903, lxxxiii, 530.

³ Claude. *Bull. Soc. Anat.*, Paris, 1896, lxxi, 502; *Med. Week*, Paris, 1897, v, 309.

⁴ Hunter, W. *Trans. Path. Soc.*, Lond., 1890, xli, 105.

⁵ Kehr. *Gall-Stone Disease*, p. 223, American translation, 1901.

all small parts

l.c.f

After intravenous injection of solution of chlorinated soda (Dakin's solution)
into dogs causes acute cholecystitis (Mann).
1) Clinically antityphoid inoculation may cause a relapse of former cholecystitis



cystic duct of which was blocked by a single calculus. Berger¹ reports two somewhat similar cases.

Forms of Acute Cholecystitis.—There are several forms of acute cholecystitis; the least severe is serous or catarrhal cholecystitis. In suppurative cholecystitis the gall-bladder is the site of an acute purulent inflammation. Midway between these two, and somewhat difficult to include in either, is simple chronic empyema of the gall-bladder, in which a chronic infection of the gall-bladder gives rise to the gradual formation of pus. This chronic suppurative cholecystitis is clinically more allied to dropsy of the gall-bladder, and is referred to again as one of the sequels of acute catarrhal cholecystitis (p. 613). The most severe forms of acute cholecystitis are the phlegmonous and gangrenous.

These three forms—catarrhal, suppurative, and phlegmonous—constitute an ascending series in the severity of the inflammation, but they merge into each other so that a distinction between any two of them may be difficult.

ACUTE CATARRHAL INFECTIVE CHOLECYSTITIS

Under this heading are included acute inflammations of the gall-bladder which stop short of ~~the production of pus~~. Different results of inflammation are here grouped together. In some instances there is only a serous exudation; in others it is sero-fibrinous, or ulceration may occur. ^ supuration

The causes of cholecystitis have already been described, and need not be recapitulated, but it may be pointed out that the less severe form (catarrhal) of acute cholecystitis may be produced by the same micro-organisms which, under more favourable conditions or when more virulent, set up suppurative inflammation; thus typhoidal infection of the gall-bladder may give rise to a simple serous cholecystitis or to a severe suppurative inflammation.

Morbid Anatomy.—The gall-bladder is distended and its walls are tense; the serous coat may be congested, dulled from the presence of fibrin, and adherent to adjacent parts. In severe cases the coats of the gall-bladder are swollen from infiltration and softened. The mucous membrane is congested, covered with mucus, and may be ulcerated or shew a deposit of bile on its surface. The cystic duct is often closed by swelling of its mucous membrane, or, as the result of past inflammation and ulceration due to the passage of a calculus, may be permanently obliterated. The cystic duct, however, is not necessarily closed. The contents of the gall-bladder may be practically clear and like serum when the cystic duct has been blocked for some time, or consist of sero-fibrinous or bile-stained turbid fluid. There may be gall-stones or inspissated bile. The lymphatic glands in relation to the cystic and common bile-ducts are enlarged. When recurrent attacks of acute cholecystitis occur the glands may become so hard as to imitate malignant infiltration, when felt during an operation. It has been urged that inflammation commonly

¹ Berger. *Arch. f. klin. Chir.*, 1907, lxxxiii, 7.

spreads from the gall-bladder to the pancreas by means of the lymphatics (Maugeret¹).

Microscopically the villousities of the mucous membrane are prominent, and the epithelial cells are desquamating and contain myelin granules. The mucous glands in the walls are dilated and inflamed, and the vessels are engorged. The fibro-muscular layers are swollen and may shew small-celled infiltration.

Clinical Features.—Acute catarrhal cholecystitis probably varies a good deal in its severity in different cases and in different infections. Many of the slighter examples never come under observation, while others are entirely overlooked or are regarded as dyspepsia, colic, etc.; in many of these cases the symptoms are not sufficiently marked to allow of accurate diagnosis. Acute cholecystitis is very likely to escape detection when it occurs in typhoid fever. The abdominal signs, pain, etc., may be thought to be due to the original disease, and the patient, from mental torpor, may not complain of pain in the region of the gall-bladder. The frequency with which the gall-bladder is found to be adherent to the stomach or colon without any evidence of chronic inflammation supports the belief that acute cholecystitis is by no means uncommon. Another argument is that gall-stones are usually due to a past attack of cholecystitis and that in many cases of cholelithiasis there is no history of such an acute attack.

The signs and symptoms of acute cholecystitis are by no means constant, and in this respect the clinical picture of acute cholecystitis resembles that of appendicitis.

In a well-marked case the earliest and most prominent symptoms are local pain and tenderness. The character of the pain may vary: in most instances it is paroxysmal and resembles that of gall-stone colic, but is less excruciating. The pain is probably due to spasmodic contractions of the gall-bladder. In a case recorded by Solieri² the biliary colic was thought to be due to blood-clot in the gall-bladder. The pain may be continuous from inflammation of the serous coat and dull. It may shoot down into the right iliac fossa and be so definitely localised there as to suggest appendicitis. This has been thought to be due to peritoneal adhesions between the gall-bladder and the appendix (Tripier and Paviot³). It is not surprising that cases of cholecystitis are often diagnosed and operated upon as appendicitis. Cholecystitis and appendicitis may coexist (*vide* p. 604).

There is tenderness over the upper right quadrant of the abdomen, which becomes localised and more intense at the so-called biliary point below the tip of the ninth costal cartilage. Cutaneous hyperaesthesia may be present in the eighth and ninth dorsal segments (Head⁴); Elsberg and Neuhof⁵ found it in 18 out of 21 cases. There is rigidity

¹ Maugeret. *Thèse de Paris*, 1908. ² Solieri. *Rev. de chir.*, Paris, 1911, xliii, 482.

³ Tripier et Paviot. *Semaine méd.*, 1903, xxiii, 29.

⁴ Head. *Brain*, Lond., 1893, xvi, 76.

⁵ Elsberg and Neuhof. *Am. Journ. Med. Sc.*, Phila., 1908, cxxxvi, 690.

The liver nearly always shows small cell infiltration of the portal spaces (Graham)

or extravasation of blood.

In a few instances copious effusions of bile into the peritoneal cavity without any rupture of the bile passages have been associated with cholecystitis. Johansson who has collected 5 examples suggests that the effusion may be connected with the occasional presence of hernial protrusions of the mucosa through the walls of the gall-bladder (Canals of Luschka).

It has been urged that haemolytic and other micro-organisms in the wall of the gall-bladder may cause pernicious anaemia (Jones and Joyce)

JOHANSSON. Rev. de chir., Part., 1912, XLVI, 892.

SCHERIN. Mitt. d. Grönl. d. med. u. chir., JENA, 1913, XXV, 197

Monziols et Collignon. Bull. et mem. Soc. med. d'exp. de Paris, 1920, 3^e s^{er}ie, XLII, 460

Fleissinger. Ibid., 1920, 6 506
Jones, N.W. and Joyce, T.M. Amer. Journ. Med. Sc., Phila., 1924, CLXXVI, 469

of the upper part of the rectus muscle and of the costal arch on the right side. Monsarrat¹ insists on the shallow jerky respiration in acute cholecystitis. The gall-bladder may be felt and sometimes seen as a pear-shaped tumour, fluctuating or tense, which usually moves with respiration and can be displaced laterally like a pendulum. It may, however, be fixed by old adhesions. The distension of the gall-bladder is due to inflammatory exudation which cannot escape because the cystic duct is occluded by swelling of the mucosa. As the inflammation subsides, the fluid discharges through the cystic duct and the tumour disappears. There may be distinct tenderness, but no palpable tumour, in the position of the gall-bladder, which is concealed by intestines in a condition of paralytic distension due to peritonitis spreading from the gall-bladder. From this tympanitic distension the right hypochondrium and epigastrium may become somewhat prominent.

Halsted² recorded a case in which sharply localised paralytic dilatation of the first part of the duodenum and pyloric end of the stomach, corresponding to circumscribed peritonitis, was found at an operation for gall-stones. The paralysed bowel was glued to the gall-bladder by recent exudation. The walls of the gall-bladder were white and thickened, and its cavity contained fluid like white of egg.

Local peritonitis around the gall-bladder often sets up vomiting, and acute intestinal obstruction may arise (Robson,³ Richardson⁴) from paralysis probably of the hepatic flexure of the colon. The symptoms usually pass off without surgical interference.

The liver is not enlarged unless the inflammation has spread to the ducts, and so into the organ. Elongation of the lower part of the right lobe covering the gall-bladder (Riedel's lobe) is met with as the result of gall-stones and past or chronic cholecystitis, and so might be present when an acute attack supervenes in these conditions. Jaundice is not a necessary accompaniment of cholecystitis; Kehr,⁵ indeed, emphasises its rarity. It may depend on an extension of inflammation and spasm to the ducts or on ~~the presence of some~~ obstruction in the ducts. In the mild degrees of serous and catarrhal cholecystitis the temperature is usually normal. But if the inflammation is severe or extends to the ducts or to the peritoneal coat of the gall-bladder, there may be fever, sometimes of such a degree as to suggest suppuration, which, however, as shewn by operation, is not present.

In rare instances micro-organisms absorbed from the gall-bladder may give rise to appendicitis (Dieulafoy⁶), endocarditis (~~Lorrain⁷~~), or infection of the urinary tract with *B. coli*.

either *B. coli*
(Monsarrat)
or
B. typhosus
(Dieulafoy)

Septicæmia
and meningitis
(SEVERIN)

¹ Monsarrat. *Practitioner*, Lond., 1908, lxxx, 775.

² Halsted. *Johns Hopkins Hosp. Bull.*, Balt., 1900, xi, 1.

³ Mayo Robson. *Med.-Chir. Trans.*, Lond., 1895, lxxviii, 117.

⁴ Richardson. *Boston Med. and Surg. Journ.*, 1899, cxli, 662.

⁵ Kehr. *Diagnosis of Gall-stone Disease*, p. 39, American translation, 1901.

⁶ Dieulafoy. *Presse méd.*, Paris, 1903, p. 445.

⁷ Lorrain. *Bull. Soc. Anat. Paris*, 1903, lxxviii, 527; LENHARTZ. *Die septischen ERKRANKUNGEN*, 1903

Diagnosis.—An enlarged gall-bladder must be distinguished from a floating kidney, hydronephrosis, renal tumour, and impacted faeces in the colon. Recurrent attacks of cholecystitis with distension of the gall-bladder may imitate intermittent hydronephrosis with Dietl's crises. The differential diagnosis of a distended gall-bladder from other conditions is given on p. 745.

The diagnosis from *suppurative cholecystitis* may be difficult, as no hard-and-fast line separates the more acute cases of cholecystitis without actual pus formation from the slighter cases of suppurative cholecystitis. Acute cholecystitis may be the early stage of the suppurative form. Clinically the difference between acute catarrhal and suppurative cholecystitis is one of degree, the pain, tenderness, and constitutional symptoms being much more marked in the latter.

From *biliary colic*, which is probably always accompanied by some cholecystitis, the diagnosis may also be very difficult. The pain is more excruciating in gall-stone colic, while the signs of local mischief, such as tenderness, paralytic distension of the intestines, or a palpable gall-bladder, are more prominent in acute cholecystitis.

The milder cases of acute cholecystitis are sometimes secondary to acute cholangitis by extension; in such cases the aspect of the disease is that of catarrhal jaundice, the existence of cholecystitis being determined only by tenderness over the gall-bladder, which may, perhaps, be palpably enlarged.

A mistake which is very easily made is to regard as *appendicitis* a case of cholecystitis, especially when the gall-bladder is dilated or so elongated as to reach the right iliac fossa, or when the right lobe of the liver is prolonged into a Riedel's lobe. Peritoneal adhesions between the two organs, to some extent, explain why in some cases of cholecystitis the pain is referred to the position of the vermiform appendix. A palpable tumour with a rounded edge directed upwards points to appendicitis; a tumour continuous with the liver dulness with a rounded edge below points to cholecystitis. It is much less often that the converse mistake is made, and a case of appendicitis is regarded as cholecystitis. But when the vermiform appendix runs up so as to come into close contact with the right lobe of the liver or even the gall-bladder, appendicitis may imitate cholecystitis very closely. It should also be remembered that acute inflammation of the appendix and of the gall-bladder may coexist (*vide* p. 604).

Acute pyelonephritis on the right side, due to infection with *B. coli*, may exactly imitate acute cholecystitis. The presence of pus in the urine should point to the kidney. But here again there may be infection of both organs by *B. coli*.

Prognosis in the milder cases is good, and the inflammatory process tends to subside rapidly. It is, however, probable that gall-stones will result, and that recurrent attacks of acute cholecystitis and of pain resembling biliary colic may occur subsequently. In the more severe attacks the danger of ulceration and perforation must be faced,

Glover report acute appendicitis in a fetally placed
caecum which imitated cholecystitis

Glover, L. R. Journ. Am. Med. Assoc., 1926, LXXV, 2093



and the prognosis is much the same as in acute suppurative cholecystitis.

Sequels.—Some cases of *serous distension* (hydrops) of the gall-bladder may be due to transient and mild infective cholecystitis, in which a calculus at the neck of the gall-bladder prevents the exit of the inflammatory exudation through the cystic duct (Kehr¹).

Chronic or Simple Empyema of the Gall-bladder.—Acute cholecystitis may become suppurative rapidly, so that the process is, for all practical purposes, suppurative cholecystitis throughout; or the symptoms of acute inflammation may pass off and be followed by a chronic infection which leads to a collection of pus inside the gall-bladder—simple or chronic empyema of the gall-bladder. These cases might be regarded as suppurative cholecystitis, but their clinical course is much more like hydrops or mucocele of the gall-bladder. They bear the same relation to acute suppurative cholecystitis that a chronic abscess does to an acute one. These cases may have a history of acute cholecystitis. Later there are abdominal pain, a tumour, malaise, loss of appetite, some wasting, and usually absence of fever. Simple empyema of the gall-bladder may intermit, the swelling passing away and then recurring.

In a man under my care gall-stones were associated with early primary carcinoma and chronic empyema of the gall-bladder. The temperature while under observation never rose above 99° F.

Ulceration of the gall-bladder may occur without any suppuration. In rare instances ulceration may lead to extensive haemorrhage.

A man aged thirty-five years, with slight jaundice, died from pneumonia and pericarditis. At the necropsy pressure on the gall-bladder, which was distended, caused practically pure blood to flow from the biliary papilla. The gall-bladder contained 2½ ounces of blood clot, its internal surface was intensely congested, shaggy, and there were some ulcers, one of which had eroded a vessel. Bacteriological examination of the gall-bladder shewed pneumococci. The kidneys weighed 3 ounces each, and were “contracted white.” The liver shewed multilobular cirrhosis. The small intestines contained blood.

Acute cholecystitis may lead to *chronic cholecystitis*, which may take one of four forms (*vide* p. 624): (1) The atrophic sclerosing, with great thickening of the walls of the gall-bladder which ultimately contracts and becomes shrivelled up. (2) The catarrhal form, in which there is a distended gall-bladder containing thick, ropy mucus. Calculi are very prone to be produced by this process. (3) Chronic ulcerative. (4) Chronic empyema, described above.

Adhesions may form between the gall-bladder and the colon, pylorus, or duodenum, and give rise to “adhesion dyspepsia,” pyloric stenosis, and dilatation of the stomach. These results are described under the morbid results of cholelithiasis (p. 758).

¹ Kehr. *Diagnosis of Gall-stones*, p. 32, American translation, 1901.

Treatment.—The patients should be kept in bed on a nourishing and easily digestible diet, and local pain treated by hot fomentations, dry cupping, or, if severe, by the application of leeches. If the pain is unbearable, morphine hypodermically may be necessary; but it masks the symptoms and should, therefore, be given with reluctance. Sickness should be controlled by effervescent draughts, bismuth, dilute hydrocyanic acid, chloretone (gr. v.) in a cachet, cocaine ($\frac{1}{10}$ -grain), or by fractional ($\frac{1}{20}$ -grain) hypodermic injections of morphine. In cases in which the temperature is high and there are signs of constitutional disturbance and the area of local peritonitis is increasing, surgical interference will probably be required. In milder cases ^{hexamine} ~~atropin~~ and salicylate of sodium, ~~or the combination of these drugs, califormin~~, should be given, in order to disinfect the ducts and increase the flow of bile and so prevent extension of inflammation from the gall-bladder to the ducts. Solis-Cohen¹ recommends succinate of sodium, and Reichmann² methylene-blue ($\frac{1}{2}$ – $1\frac{1}{2}$ grains) in capsules. A mild laxative should be given to keep the bowels open and to favour evacuation of the inflammatory contents of the gall-bladder. ~~Vaccine treatment with *Bacillus coli* gave good results in 2 cases in which sinuses persisted after operations for gall-stones (Wright and Reid³).~~ The after-treatment is that of the prophylaxis of gall-stones (*vide* p. 773).

MEMBRANOUS CHOLECYSTITIS

Synonyms: Croupous Cholecystitis; Fibrinous Cholecystitis.

Inflammation of the gall-bladder may give rise to the formation of a cast of its cavity, which to the naked eye resembles the casts in mucous colitis (membranous colitis). As long ago as 1818 Richard Powell⁴ described attacks of colic followed by jaundice in patients whose faeces contained membranes, but no calculi. Membranous cholecystitis, of which few cases are on record, is usually associated with gall-stones.

Cases of biliary colic accompanied by membranes in the stools have been described by Mayo Robson⁵ and by P. C. Fenwick.⁶ In one of Mayo Robson's cases 78 calculi were afterwards removed from the gall-bladder, and Fenwick's patient had almost certainly passed gall-stones previously. In a case operated upon at St. George's Hospital a fibrinous cast of the gall-bladder surrounding a single large calculus was found.⁷ In a case operated upon by Moynihan⁸

¹ Solis-Cohen. *Proc. Phila. County Med. Soc.*, xxiii, 36.

² Reichmann. *Semaine méd.*, Paris, 1903, xxiii, 140.

³ Wright and Reid. *Brit. Med. Journ.*, 1906, i, 142.

⁴ Powell, R. *Med. Trans. Coll. Physicians, Lond.*, 1820, vi, 106

⁵ Robson, Mayo. *Diseases of the Gall-bladder and Bile-ducts*, p. 79, 3rd ed., 1904.

⁶ Fenwick, P. C. *Brit. Med. Journ.*, 1898, i, 1072.

⁷ Rolleston. *Trans. Path. Soc., Lond.*, 1902, liii, 405.

⁸ Moynihan. *Brit. Med. Journ.*, 1903, i, 186.

Hurst on the view that hexamine irritates the urinary bladder only when the urine is acid by liberating formalin gives a single dose at night of potassium citrate 3i, sodium salicylate grsxx, and hexamine grsxx which is increased by grains x every night up to grains lx to xc or until signs of vesical irritation appear.

Lyon's method of non-surgical drainage of the biliary tract consisting in the passage of a duodenal tube with which the region of the biliary papilla is sprayed with a 33 per cent. solution of magnesium sulphate so as to relax Oddi's sphincter and allow aspiration of the bile has been much practised and discussed.

According to Hurst 1 to 4 drams of magnesium sulphate in a concentrated solution taken half an hour before a meal relaxes Oddi's sphincter just as well as the intra-duodenal spray. A vaccine from the predominant microorganisms in the bile may be tried.

HURST, A.F. Practitioner, London, 1923, CXI, 321

LYON, B.V.V. Non-Surgical Drainage of the Gall Tract, 1923



368 calculi were removed; and Bland-Sutton¹ mentions a case with calculi. In 2 cases mentioned by Walton² gall-stones were absent.

Microscopically in the case I examined there was a fibrinous network enclosing bile-pigment and hexagonal and quadrilateral crystals. In the outer layers of the cast there were round-cells, but no trace of the mucous membrane of the gall-bladder was found. The fibrinous structure differs entirely from the microscopic appearances of the casts passed in mucous colitis. Microscopical examination will distinguish it from sloughing of the mucous membrane of the gall-bladder.

Clinically the symptoms are those of gall-stone colic, from which it can be distinguished only by finding membranous casts instead of calculi in the motions. The condition may be found only when the gall-bladder is open in the course of an operation, as in the following case:

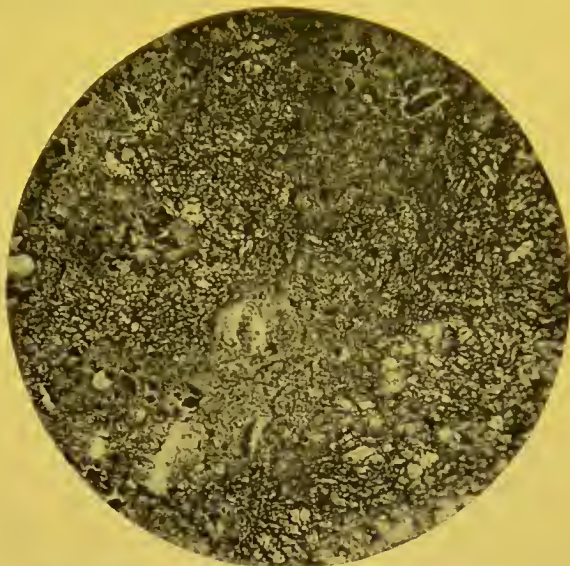


FIG. 82.—Photomicrograph of cast from the gall-bladder, shewing fibrinous network enclosing masses of black bile-pigment. (By Dr. S. G. Penny.)

A woman aged fifty-two, who had never had jaundice or biliary colic, was seized with pain in the right side of the abdomen and vomiting on November 14, 1900. On admission two weeks later a tumour of stony hardness was found in the right iliac fossa, separated by a zone of resonance from the liver dulness. It was thought to be probably carcinoma of the colon. Laparotomy revealed a greatly enlarged gall-bladder with adhesions to adjacent parts. It contained a single gall-stone, rather bigger than a walnut, enclosed in a thick fibrinous sac about $\frac{1}{4}$ inch thick. The calculus and the cast were removed, but the gall-bladder was left. This envelope was quite distinct and easily separable from the lining of the gall-bladder. The microscopical appearances are described above (Fig. 82). The patient made a good recovery.

The *treatment* of an attack is the same as that of gall-stone colic, but if attacks recur, the gall-bladder should be opened and calculi removed. Moynihan considers that the gall-bladder should be removed, but it is doubtful if there are as yet sufficient grounds for this dictum.

Acute Haemorrhagic Cholecystitis is occasionally seen. The condi-

¹ Bland-Sutton. *Gall-stones and Diseases of the Bile-ducts*, p. 30, 1907.

² Walton. *Ann. Surg.*, 1911, liv, 176.

tion is one of acute infective inflammation and resembles the more severe forms of acute cholecystitis in its general connections, symptoms, and results.

SUPPURATIVE CHOLECYSTITIS

In this condition inflammation of the walls of the gall-bladder gives rise to an accumulation of pus in its cavity and may go on to ulceration and perforation. Two conditions have in common the production of pus inside the gall-bladder, but differ in their clinical course and aspects. In one—chronic empyema of the gall-bladder—pus is slowly formed within the gall-bladder, and its features are much the same as those of distension of the gall-bladder with mucous fluid (dropsy of the gall-bladder). In the other there is an acute suppurative inflammation. Except where specially stated, the following description refers to the latter condition. Chronic empyema is referred to on page 613. It is difficult to draw a hard-and-fast line between the less severe cases of acute suppurative cholecystitis and chronic empyema of the gall-bladder. When very acute, suppurative cholecystitis is described as phlegmonous cholecystitis.

The causes of suppurative cholecystitis are much the same as those of cholecystitis in general, and need not be repeated in detail. It is frequently associated with gall-stones. In 55 cases of suppurative cholecystitis collected by Courvoisier 41 were associated with cholelithiasis. Impaction of a calculus in the cystic duct or neck of the gall-bladder favours infection, as any micro-organisms reaching the gall-bladder by the blood-stream are retained and able to multiply. It is possible that in some cases of suppurative cholecystitis a calculus may have been previously expelled, but the presence of gall-stones is no more necessary than are enteroliths in appendicitis. Obstruction of the cystic or common bile-duct may act in a similar manner. Primary carcinoma of the bile-ducts may thus become complicated by suppurative cholecystitis.

Carcinoma of Cystic Duct; Round Worm in Common Bile-duct; Suppurative Cholecystitis.—A woman, aged forty-three, after long-continued and vague pains suggesting biliary colic, became intensely jaundiced, developed a high temperature, and died. There were gall-stones in the gall-bladder and suppurative cholecystitis due to a member of the colon group, primary carcinoma completely obstructing the cystic duct, and a dead lumbricoid worm in the common bile-duct, which, it was thought, had conveyed the infection (Étienne¹). I have seen acute haemorrhagic cholecystitis associated with early carcinoma of the cystic duct.

Suppuration may spread into the gall-bladder from suppurative cholangitis due to various causes, such as the rupture of a hydatid cyst

¹ Étienne. *Arch. gén. de méd.*, Paris, 1896, clxxviii, 284.



Halstead ~~has~~ pointed out that the edge of the liver is turned up over an acutely distended suppurating gall-bladder and may be felt as a ridge. The liver is often enlarged from infection & pericholangitic infiltration (E. Graham)

Halstead. Bull. Johns Hopkins Hosp., Baltimore
1920, xxxi, 14.
GRAHAM, E. Surg., Gyn. & Obst., 1916, xxvi, 521.

into the ducts. In enteric fever suppurative cholecystitis may occur, but fortunately it is rare, and is not so often seen as catarrhal cholecystitis.

Among 620 cases of enteric fever observed during seven years at Montreal there was 1 case of suppurative cholecystitis.¹ In 2000 fatal cases at Munich tabulated by Hölscher there were 5 of cholecystitis with suppuration.² In 1016 cases of enteric fever treated during 1900–1901 in the Imperial Yeomanry Hospitals in South Africa there was 1 case of suppurative cholecystitis. Thus, among 3636 cases of enteric fever there were 7 cases of suppurative cholecystitis, or 0·2 per cent.

Morbid Anatomy.—The gall-bladder is usually enlarged, sometimes very considerably; but suppuration may occur in a gall-bladder shrivelled up and contracted from recurrent cholecystitis. The peritoneal coat is inflamed, granular from adherent lymph, and usually darkish-red or greenish-black in colour. It may be adherent by old fibrous adhesions to the parts around, or glued to them by recent lymph. Inflammation may thus spread to adjacent coils of intestine and cause paralytic distension. The wall of the gall-bladder is swollen from inflammatory exudation, softened, and friable. The mucous membrane is largely destroyed, the free surface shews granulation-tissue and is shaggy, red, and in places has flakes of adherent lymph. Microscopically there is extensive small-celled infiltration of the walls. Ulceration is commoner near the fundus, because calculi are more likely to gravitate there. The contents are bile-stained or sanious pus, and calculi are often present. In chronic empyema the wall of the gall-bladder is thickened from organisation of the inflammatory exudation.

Clinical Picture.—The signs and symptoms vary considerably. They may be local, and at first confined to the region of the gall-bladder, or general, from widespread infection of the peritoneum.

The local manifestations are pain, tenderness, increased resistance of the overlying rectus abdominis muscle and rigidity of the upper part of the right costal arch. In cases in which the abdominal muscles are extremely atrophied there may be no spasm or rigidity. The abdominal reflex may be impaired or absent on the right side (Jamin³). The gall-bladder may be palpable as a tense, pear-shaped tumour, in a line between the tip of the ninth rib and a point one inch below the umbilicus in the middle line (Mayo Robson). The gall-bladder varies in shape: when elongated, it may appear to be independent of the liver, since it may be separated from the liver dulness by a zone of resonant intestines. In a case of pyopneumocholecystitis, in which the gall-bladder communicated with the colon, the gall-bladder formed a large tympanitic tumour (Pende⁴). A somewhat similar case in which there was a

¹ Stewart, J. *Brit. Med. Journ.*, 1901, i, 1463.

² Hölscher. *München. med. Wchnschr.*, 1891, xxxviii, 43.

³ Jamin. *Deutsche med. Wchnschr.*, 1904, xxx, 1088.

⁴ Pende. *Policlin.*, Roma, 1907, xiv, 540.

communication with the duodenum is mentioned by Mayo Robson.¹ When suppuration occurs in a gall-bladder already considerably distended, the tumour may be palpable in the right iliac fossa and may suggest appendicitis. In such cases the right lobe of the liver is often elongated (Riedel's lobe). In exceptional instances the gall-bladder is found in the middle line of the abdomen. When there is local peritonitis around the gall-bladder, intestinal paralysis and distension may prevent its being felt, but the hypochondrium will be prominent and exquisitely tender. In other cases rigidity of the abdominal muscles prevents the gall-bladder from being made out, unless the examination is made under an anaesthetic. In many instances the gall-bladder is contracted from past inflammation, and though acutely inflamed and containing pus, does not project beyond the margin of the right lobe.

Pain is constant, as a rule; but exacerbations of great severity resembling biliary colic may occur, and its intensity varies considerably in different cases. It is usually felt in the right hypochondrium or pit of the stomach, but may be referred to the right iliac region. The temperature is raised and may be high, and be accompanied by rigors. The pulse is rapid (100–120). An increasing pulse-rate calls for operative interference. There may be vomiting, from the irritation of the peritoneum around the gall-bladder, and the local peritonitis thus produced may spread to neighbouring coils of the small intestines, or to the hepatic flexure of the colon, and lead to paralysis of the bowel and so to the symptoms of intestinal obstruction. Jaundice is very commonly absent, and when present is usually slight. It may be due to extension of inflammation into the common bile or hepatic ducts, or to definite causes of biliary obstruction, such as gall-stones or tumours involving the extra-hepatic bile-ducts. It has been suggested that when the mucous membrane of the gall-bladder is ulcerated, bile may be absorbed from the gall-bladder, and that slight icterus in the early stages of suppurative cholecystitis, before the cavity becomes filled with pus, may be due to this cause, but this is unlikely.

The spleen is occasionally enlarged. Albuminuria may be present in severe cases, and is due to the local action on the renal epithelium of poisons absorbed from the gall-bladder; in very rare cases temporary toxic glycosuria may appear (Mansell Moullin²). There is leucocytosis of from 15,000 to 30,000; when the infection is a pure culture of *B. typhosus*, leucocytosis has been said not to occur (Findlay and Buchanan³); but M'Crae⁴ found a count of from 10,000 to 15,000. According to Libman,⁵ blood-cultures are negative unless there is also cholangitis. In rare instances there is pus in the urine from a concomitant infection of the renal pelvis with *B. coli*. In severe cases there may be nothing to indicate that the gall-bladder is the organ at fault, the symptoms being

¹ Robson, Mayo. *System of Medicine* (Allbutt and Rolleston), 1908, iv, part i, 244.

² Mansell Moullin. *Lancet*, 1907, i, 1645.

³ Findlay and Buchanan. *Glasgow Med. Journ.*, 1906, lxx, 189.

⁴ M'Crae. *System of Medicine* (Osler and M'Crae), 1907, ii, 137.

⁵ Libman. *Am. Journ. Med. Sc.*, Phila., 1908, cxxxvi, 548.

When suppuration extends out of the gall-bladder and tension is relieved, pain may disappear and the pulse and temperature become normal, though a leucocytosis persists.

General infection may follow,
and local lesions such as
endocarditis and meningitis (SEVERIN)

SEVERIN. Mitt. a. d. Grenzgeb. d. Med. u. Chir., JENA,
1913, XXV, 797

those of general peritonitis or intestinal obstruction, and thus imitating those due to perforation of the intestine or appendix. If operation is delayed, the localising symptoms present in an early stage become masked by general peritonitis.

Complications and Results.—The chief danger is perforation into the general cavity of the peritoneum and fatal peritonitis.

Keen¹ collected 31 examples of perforation due to typhoidal cholecystitis; of these, 26 were not operated upon and all proved fatal; 5 were operated upon, with 3 recoveries.

Perforation of the gall-bladder may lead to a local peritoneal abscess instead of to general peritonitis. The formation of a local abscess is favoured by the presence of previous peritoneal adhesions shutting off the cavity of the general peritoneum. The abscess may imitate other forms of local abdominal suppuration, such as a subdiaphragmatic abscess due to disease of the stomach, duodenum, or pancreas, or malignant disease of the gall-bladder (Tuffier²). The abscess may discharge into the stomach, duodenum, colon, or penetrate the diaphragm and cause an empyema or a broncho-biliary fistula; or it may open through the skin close to the costal arch or at the umbilicus. In rare instances the abscess may communicate with the pelvis of the right kidney, or even the bladder or vagina. A suppurating gall-bladder may ulcerate directly into the liver and give rise to an abscess continuous with the cavity of the gall-bladder.

Weir³ records the case of a woman aged thirty-five whose gall-bladder contained 3 ounces of pus. Ulceration on the anterior wall of the gall-bladder led into an abscess in the liver containing more than an ounce of pus. A woman aged fifty-three died in St. George's Hospital with multiple recurrent growths after removal of the mamma; the cystic duct was blocked by a calculus; the gall-bladder contained pus and communicated by two openings with a small abscess in the liver. Suppuration in a gall-bladder deeply embedded in the liver substance, the so-called intrahepatic gall-bladder (*vide* p. 602), would imitate hepatic abscess.

Concomitant suppurative cholangitis may lead to multiple areas of suppuration in the liver; these readily infect the hepatic veins, induce secondary abscesses in the lungs, which may burst into the pleura and set up empyema. Profuse haemorrhage into the gall-bladder from ulceration of the vessels is very rare; jaundice increases the tendency to haemorrhage.

Appendicitis may complicate suppurative cholecystitis, and in operating on cholecystitis the condition of the appendix should be investigated, as in such a case death may subsequently occur from perforation of the

¹ Keen. *Complications and Sequels of Typhoid Fever*, pp. 249, 325, 1898.

² Tuffier. *Bull. et mêm. Soc. de chir. de Paris*, 1911, xxxvii, 1343.

³ Weir. *Med. Rec.*, N.Y., 1900, lvii, 1137.

appendix. The cholecystitis may be secondary to infection from the appendix or *vice versa* (Dieulafoy¹).

Diagnosis.—Before perforation has occurred suppurative cholecystitis resembles other forms of local peritonitis in the neighbourhood, such as might be set up by a duodenal ulcer before perforation, by a localised subphrenic pneumothorax, or to an abnormally situated appendicitis. In addition to the signs of local peritonitis the presence of a tumour moving with respiration in or near the situation of the gall-bladder is an important indication of cholecystitis. Absence of jaundice does not militate against the existence of cholecystitis, though the history of past attacks of biliary colic with transient jaundice strengthens the diagnosis.

In duodenal ulcer there should be a history of pain about two hours after food, but, unfortunately, the ulcer may remain latent until it perforates and sets up general or localised peritonitis. There may be considerable resemblance between the two conditions; I have seen two cases in which perforating duodenal ulcer was diagnosed as cholecystitis; and adhesions between the gall-bladder and the duodenum, due to an ulcer, may present a very puzzling problem in diagnosis (Hinder²).

A localised subphrenic abscess due to perforation of a gastric ulcer hardly ever imitates suppurative cholecystitis, as the abscess is nearly always gaseous (a subphrenic pyopneumothorax); but in the following case the absence of resonance led to an open diagnosis:

A woman aged twenty-eight years had sudden pain on Nov. 14, 1900. She came up to St. George's Hospital on Nov. 16, with a firm mass, tender and dull on percussion, in the position of the gall-bladder. She had no jaundice, and there was no history of gall-stone colic, but she had previously had some dyspeptic pain one hour after food. The pulse was 140, and the patient's face indicated grave abdominal mischief. The diagnosis lay between suppurative cholecystitis and a local abscess due to perforated gastric ulcer. Operation revealed a localised peritoneal abscess due to perforation of a gastric ulcer close to the pylorus.

An elongated and distended gall-bladder may project into the right lower half of the abdomen and simulate appendicitis; as already mentioned, this condition is frequently associated with an elongated right lobe of the liver. Cases of cholecystitis are not infrequently regarded as appendicitis; the converse mistake is much rarer. The differential diagnosis is very difficult, as both these conditions vary so much in their clinical manifestations (*vide* p. 612). As pointed out above, cholecystitis and appendicitis may coexist. Occasionally pneumonia or pleurisy at the right base may imitate acute cholecystitis. The resemblance of a suppurating gall-bladder to a right pyonephrosis may be extremely close.

When perforation of a suppurating gall-bladder sets up general peritonitis, the diagnosis must be made from other forms of peritonitis, especially that due to fulminating appendicitis, which it often closely

¹ Dieulafoy. *Presse méd.*, Paris, 1903, p. 448.

² Hinder. *Trans. viii. Australasian Med. Congress*, 1909, i, 317.

resembles inasmuch as the pain may be referred to the right iliac fossa, probably because the contents of the gall-bladder may travel down into the region of the appendix. The history may be of help in forming an opinion, but in either case immediate operation is essential. When the abdomen is opened the character of the exudate may indicate the perforated viscus; thus bile or calculi will direct attention to the gall-bladder; an acid reaction or gas, to perforation of the stomach or duodenum.

Prognosis.—There is little tendency to spontaneous cure by the discharge of the purulent contents through the cystic duct and subsidence of the inflammatory process, since in most cases the cystic duct is blocked or obstructed. This may be due to various factors, such as an impacted calculus, the contraction of cicatricial fibrous tissue, either as the result of past ulceration or from pericholecystic adhesions, or to new growth involving the duct. When the obstruction of the cystic duct depends on swelling of the mucous membrane, due to the spread of inflammation from the gall-bladder, it is possible that the purulent contents may be expelled through the duct. When the progress is less acute, pus may be formed in the gall-bladder and may remain confined there; this is chronic empyema of the gall-bladder. But in acute suppurative cholecystitis the inflammatory process spreads through the walls of the gall-bladder, infects the surrounding peritoneum, and leads to local or general peritonitis. In these circumstances, therefore, the prognosis is grave unless operative interference is invoked before more widespread infection has set in. A local abscess may be treated surgically very successfully, but if general peritonitis has supervened the outlook is very gloomy.

Treatment.—The proper treatment of suppurative cholecystitis and of the more chronic condition, empyema of the gall-bladder, is surgical and consists in opening the gall-bladder and draining it, or, if it appear necessary, removing it. Exploratory puncture through the abdominal walls with a syringe is dangerous, and should never be countenanced. The palliative or medical treatment is the same as in acute cholecystitis.

PHLEGMONOUS CHOLECYSTITIS

This is a very acute infective form of cholecystitis, and differs only in degree from the acute suppurative form just described. It passes into gangrenous cholecystitis, from which again it can hardly be separated; in fact, gangrene is merely a result of phlegmonous cholecystitis.

It may supervene on the same conditions as suppurative cholecystitis, such as cholelithiasis, typhoidal cholecystitis (Schlier,¹ Wunschheim,²), and is due to a very virulent infection.

Incidence.—Comparatively few cases are on record, but probably many cases described as acute suppurative cholecystitis might be included under this heading. Courvoisier, who first described it as acute pro-

¹ Schlier. *Deutsch. Arch. f. klin. Med.*, 1891, xlviii, 441.

² Wunschheim. *Prag. med. Wchnschr.*, 1898, xxiii, 13.

gressive empyema of the gall-bladder, collected 7 cases; Mayo Robson¹ added 5 more; Wright² met with 3 cases in a few years.

Morbid Anatomy.—The changes are the same as in acute suppurative cholecystitis, but more extensive and acute. The outside of the gall-bladder is purple, oedematous, and inflamed with adherent lymph. The walls are swollen, friable, and infiltrated with pus and blood; the mucous membrane is swollen, and may be ulcerated, necrosed, or be separated in flakes from the underlying coats. The gall-bladder contains pus and often gall-stones. The cystic duct is closed and may be blocked by a calculus.



FIG. 83.—Gall-bladder with a large calculus in its neck. Phlegmonous inflammation passing into gangrene. (Drawn by Dr. E. A. Wilson.)

Clinical Features.—Symptoms set in suddenly with pain in the region of the gall-bladder. The peritoneum early becomes involved, at first locally, but soon peritonitis becomes generalised, unless there are firm adhesions around the gall-bladder.

Jaundice may be present from concomitant inflammation of the ducts, but it is inconstant, and therefore of no great diagnostic value. The results are marked toxaemia, peritonitis, ulceration, sloughing, perforation, and gangrene of the gall-bladder, leading to localised or generalised peritonitis.

The diagnosis depends on evidence of acute inflammation in the region of the gall-bladder in a patient whose history points to past cholecystitis. In some cases there may only be evidence of general peritonitis with or without the history that it followed localised inflammation in the right upper quadrant of the abdomen. When there is more or less localised inflammation of the peritoneum in the right

upper half of the abdomen, the differential diagnosis is the same as in other forms of cholecystitis, to which the reader should refer. It may be very difficult when general peritonitis is established to make out whether it is due to fulminating appendicitis or to cholecystitis. Perforation of a gastric or duodenal ulcer, acute intestinal obstruction, or acute pancreatitis, may be imitated. The accurate diagnosis of phlegmonous cholecystitis is extremely difficult; this is shewn by the following case, in which there was a transition from phlegmonous to gangrenous cholecystitis.

A woman aged sixty-three was admitted into St. George's Hospital with a history of constipation for three days and of more acute symptoms and vomiting

¹ Robson. *Diseases of the Gall-bladder*, p. 90, 1904; *Brit. Med. Journ.*, 1903, i, 189.

² Wright, G. A. *Lancet*, Lond., 1906, ii, 795.



Orti describes gangrene of
the gall-bladder after
influenza

Orti, A. Deutsche med. Wochenschr. 1918
XLIV, 1298

for twenty-four hours. The sac of an umbilical hernia which she had had for three years was opened, and was found to contain adherent omentum, coils of small intestine, and a piece of the colon. The bowel, which was not strangulated, was returned. She died thirty hours after the operation. At the necropsy there was general peritonitis. The gall-bladder was adherent to the colon, and contained several gall-stones in the fundus; its mucous membrane was ulcerated and necrotic, especially on the anterior surface of the gall-bladder. A large calculus, impacted in the neck of the gall-bladder, occluded the commencement of the cystic duct (*vide* Fig. 83).

The prognosis is very grave, as the disease may prove fatal in a few days, the process being so virulent that infective peritonitis is rapidly set up. The disease is too acute to allow adhesions capable of localising the infection to be formed.

The treatment is generally that of perforative peritonitis, and though the pain may be relieved by hot fomentations and the hypodermic injection of morphine, the only satisfactory measure is laparotomy and removal of the gall-bladder. Morphine should not be given until the diagnosis is made, as it masks the symptoms.

GANGRENOUS CHOLECYSTITIS

Synonym: Gangrene of the Gall-bladder.

In extremely rare instances gangrene of the gall-bladder is due to torsion (Nehrkorn,¹ Wendel²). As a rule, it is a further stage, or rather a result, of the very acute infective or phlegmonous inflammation of the gall-bladder just described; and, as already pointed out, no rigid distinction can be drawn between them. The transitional cases with small areas of necrosis in the gall-bladder may be spoken of as partial gangrene, as in Donoghue's³ case. It stands in the same relation to cholecystitis that gangrenous appendicitis does to other forms of inflammation of the appendix, but is rare, whereas gangrenous appendicitis is common. It seems probable that the comparative rarity of gangrene of the gall-bladder may in part be explained by its better blood-supply and by the fact that it is not prone, like the appendix, to be twisted on its own axis and its blood-supply thus interfered with. The factors which bear on the production of gangrene are: a highly virulent infection, interference with the blood-supply, such as thrombosis or constriction, and obstruction of the cystic duct whereby drainage is prevented and tension produced.

Incidence.—It is not nearly so rare as was formerly thought, and probably some cases have been described merely as very severe cholecystitis.

¹ Nehrkorn. *Deutsche Ztschr. f. Chir.*, Leipz., 1908, xevi, 319.

² Wendel. *Ann. Surg.*, 1898, xxvii, 199.

³ Donoghue. *Am. Journ. Med. Sc.*, Phila., 1902, exxiii, 193.

Cases have been reported by Hotchkiss,¹ Mayo Robson,² Mayo,³ Gibbon,⁴ Moynihan,⁵ Körte,⁶ Elsberg and Neuhof,⁷ Lilienthal (7),⁸ Bland-Sutton,⁹ Waring,¹⁰ and others.

The **morbid anatomy** is the same as in phlegmonous cholecystitis, with the addition of gangrene of the wall of the gall-bladder. The extent of the gall-bladder affected by gangrene varies, but it appears to begin at the fundus and spread towards the neck of the gall-bladder. The gangrenous walls are dark green in colour, extremely soft, and friable. In other cases there are scattered gangrenous patches.

The cystic duct is blocked, and there may be a calculus imbedded in the neck of the gall-bladder. Calculi are present in the gall-bladder in the vast majority of the cases.

The **clinical features** are the same as those of phlegmonous cholecystitis in a late stage—viz. general peritonitis. In fact, as already pointed out, gangrenous cholecystitis is the extreme stage of the phlegmonous form. In Gibbon's case there was a leucocytosis of 37,600, which fell to 12,600 in twenty-four hours after removal of the gall-bladder. In two cases the band of hyperaesthesia in the eighth and ninth dorsal segments was present (Elsberg and Neuhof). In a man with existing renal disease, gangrenous cholecystitis reflexly produced anuria and gave rise to a diagnosis of pyonephrosis (Elsberg and Neuhof).

The **diagnosis** is extremely difficult, and cannot be made from perforative peritonitis due to other lesions of the gall-bladder. It is very likely to be confused with peritonitis due to fulminating appendicitis.

The only **treatment** is surgical, and consists in removal of the gall-bladder (cholecystectomy). There should be no delay in operating on any case thought to be phlegmonous or gangrenous cholecystitis.

CHRONIC CHOLECYSTITIS

Chronic cholecystitis occurs in a number of forms, and there is considerable confusion in the nomenclature. Under the title *chronic catarrhal cholecystitis* Maccarty¹¹ describes a comparatively slight form in which the principal gross change is erosion of the apices of the papillae of the mucous membrane. The papillae appear as yellow specks, and from their resemblance to strawberry seeds the name "strawberry gall-bladder" has been employed. (This condition is obviously different from the form

¹ Hotchkiss. *Ann. Surg.*, 1894, xix, 197.

² Mayo Robson. *Brit. Med. Journ.*, 1903, i, 181.

³ Mayo, quoted by Gibbon.

⁴ Gibbon. *Am. Journ. Med. Sc.*, Phila., 1903, cxxv, 592.

⁵ Moynihan. *Brit. Med. Journ.*, 1903, i, 186.

⁶ Körte. *Beiträge z. Chirurg. der Gallenwege u. der Leber*, S. 108, 1905.

⁷ Elsberg and Neuhof. *Am. Journ. Med. Sc.*, Phila., 1908, cxxxvi, 690.

⁸ Lilienthal. *Mt. Sinai Hosp. Rep.*, N.Y., 1907, v, 242.

⁹ Bland-Sutton. *Gall-stones and Diseases of the Bile-ducts*, p. 29, 1907.

¹⁰ Waring. *Clin. Journ.*, Lond., 1911, xxxviii, 33.

¹¹ Maccarty. *Ann. Surg.*, Lond., 1910, li, 651.

, contain cholesterol-ester,

Among 5000 excised gall bladders 936 were strawberry
and 195 or 4 per cent, were papillomatous gall bladders (MacCarty)

and Deaver considers that inflammation
of the adjacent lymphatic glands always
preceded the pancreatitis

"Luschka's Crypts" are gland-like
spaces containing epithelial debris;
they are not found in healthy
gall bladders. They occur in large
numbers in chronic cholecystitis,
and may form calculi. The liver
almost invariably shows pericholangitic
lymphoglyc infiltration and fibrosis

Deaver, Surg. Gyn., and Obst., 1919, XXIII,
433
MacCarty and Jackson. Collected Papers of the
Mayo Clinic, 1920, XII, 102

now to be described, which, however, has often been called chronic catarrhal cholecystitis, and is named chronic cholecystitis by Macearty.

Causes.—It may be a legacy left by a past attack of acute cholecystitis, and is often associated with gall-stones. In other cases the process is probably chronic from the first, and may be disposed to by sedentary habits, constipation, tight lacing, and the other factors that favour infection of the gall-bladder. Chronic cholecystitis may be part of chronic catarrh of the ducts, and is then quite subordinate to that condition.

Morbid Anatomy.—The gall-bladder is usually somewhat distended with mucus, which may be so thick and tenacious as to resemble grains of boiled sago or aspic. It may or may not contain calculi; occasionally calculi are embedded in the walls of the gall-bladder (parietal calculi). There may be adhesions between the gall-bladder and adjacent organs, but they may be absent even when the gall-bladder contains calculi. The walls of the gall-bladder are thickened, and the inner surface is thrown into folds; but when the gall-bladder is distended as a result of a stone in the cystic duct, its walls are thin and smooth, and have a white, nacreous appearance. From contraction of inflammatory tissue the gall-bladder may become small and shrivelled up (cholecystitis obliterans). Secondary calcification of the walls sometimes occurs (Fig. 84). The cystic duct is often quite pervious. There may be chronic pancreatitis which may be due to infection by the lymphatics (Maugeret¹).

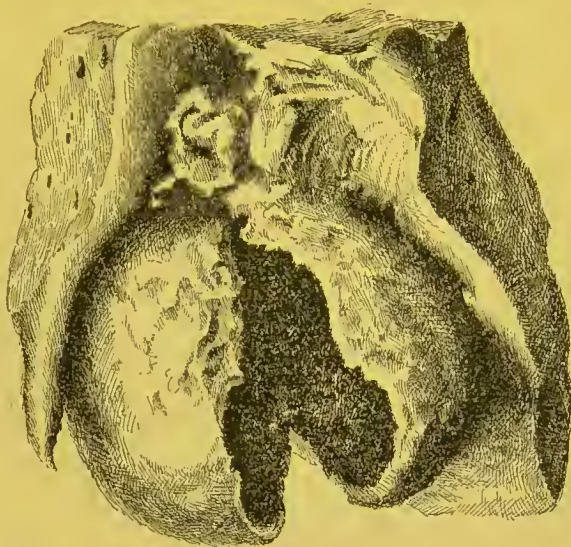


FIG. 84.—Chronic cholecystitis with calcification. From a specimen (Series ix, No. 195 A) in the Museum of St. George's Hospital. (Drawn by Dr. E. A. Wilson.)

Microscopically the thickening of the wall of the gall-bladder is due to fibrosis and proliferation of connective tissue between the muscular and serous coats. There may be much well-formed connective tissue with a little intervening small-celled infiltration. There may also be some oedema and swelling, and sometimes hyaline degeneration of the fibrous tissue. The mucosa may be replaced by scar tissue. I have not observed the elongation of mucous glands through the muscular coat to the serosa described by Ries,² and am inclined to consider such a process as evidence of early malignant disease.

¹ Maugeret. *Thèse de Paris*, 1908.

² Ries. *Ann. Surg.*, 1902, xxxvi, 503.

Clinically, the symptoms are practically those of cholelithiasis. There are attacks of biliary colic from time to time. In the intervals, when the subacute attack of inflammation has subsided, there is no jaundice and no tenderness over the gall-bladder, which can sometimes be felt as a pear-shaped tumour. Elsberg and Neuhof¹ find that cutaneous hyperaesthesia in the eighth and ninth dorsal segments is present in many cases. The distinction between chronic cholelithiasis with periodic attacks of colic and chronic cholecystitis is artificial. From an academic point of view a criterion might be made of the presence or absence of gall-stones; the cases of chronic cholecystitis associated with gall-stones



FIG. 85.—Section of wall of gall-bladder in chronic cholecystitis. The villusities of the inner coat are seen, but there is no epithelium left on the surface. The darker longitudinal strands are smooth muscle. The lighter portion, which constitutes two-thirds of the thickness of the wall, is fibrous tissue shewing oedema and some small-celled infiltration. Low power. (Photomicrograph by Dr. H. Spitta.)

might then be removed to another category and included under cholelithiasis. It is doubtful if a diagnosis between chronic cholecystitis and gall-stones can be made on the ground that the biliary colic is more severe in the case of gall-stones, since, after repeated attacks of biliary colic, the ducts may be so dilated that pain is comparatively slight. When there are no gall-stones, the attacks of colic due to subacute cholecystitis are less likely to be followed by jaundice, and no calculi can be recovered from the stools.

Arthritis and phlebitis may be secondary to

chronic cholecystitis; and I have known infection of the urinary tract with *B. coli* occur in a patient with cholecystitis. ~~Signs of~~ myocardial ^{failure} ~~insufficiency~~ may occur (Babcock²). ^{Grave}

Treatment.—The medical treatment is that of cholelithiasis, namely, a careful dietary with plenty of water, salicylate of sodium and ^{hexamidine} ~~urotropin~~, regular action of the bowels and exercise. These measures are directed to prevent stagnation of bile in the gall-bladder and to increase the flow of bile through the ducts and gall-bladder so as to flush them. Indigestion should be carefully treated so as to prevent further infection of the gall-bladder; ^{Carlsbad salts} ~~Carlsbad salts~~ before breakfast are useful for the ^{stomach} ~~purpose~~.

Surgical drainage of the gall-bladder is followed by good results.

¹ Elsberg and Neuhof. *Am. Journ. Med. Sc.*, Phila., 1908, cxxxvi, 690.

² Babcock. *Journ. Amer. Med. Assoc.*, Chicago, 1909, lii, 1904.

1) Most observers have found hypochlorhydria; but some (Griffith describes hypochlorhydria. Piercet and Boekus found diminution of the pancreatic ferments in 85 per cent. of 46 cases of cholecystitis, and consider that, like achylia, this is in favour of cholecystitis.)
The bile obtained by siphonage from the duodenum is frequently unduly pale from failure of the gall-bladder to concentrate it, and its cholesterol content has been found to be low (McClure and Vance.)

2) Chronic infective

2) M. J. Lichty

Griffith, H. E. Lancet, 1924, ii, 203.

McClure, C. W. and Vance, E. Boston Med. and Surg. Journ., 1924, cxc, 765

Piercet, G. M. and Boekus, H. L. Arch. Int. Med., Chicago, 1925, xxxv, 204.

~~Holdaway, D. Arch. Int. Med., 1912, cxiv, 255~~

Lichty, M. J. Ohio med. Journ., Columbus, 1915, xi, 779.

In the "Straasbory gall"
Kaddor Moynihan advises
cholecystectomy

A Diverticulum in the
absence of calculi may
result from an ulcer; this
may have caused the
diverticulum at the neck
of the gall bladder in
Abbott's case.

Moynihan. Brit. Med. Journ., 1913, i, 11.

Abbott, G. K. Surg., Gyn., and Obstet., 1920, xxxvi, 466.

Cholecystectomy, according to Ries, is preferable to removing the mucous membrane of the gall-bladder and leaving the rest of the viscus, as practised by Mayo;¹ and in favour of removal it may be urged that carcinoma may be present although the naked-eye appearances do not suggest it. (*Vide* p. 634.)^

Atrophic Sclerosing Cholecystitis.—*Synonym*: Cholecystitis obliterans.—This thickened, retracted condition of the gall-bladder is the result of chronic cholecystitis and is often associated with cholelithiasis of old standing. Rough calculi are probably more likely to be associated with chronic cholecystitis than smooth gall-stones. The gall-bladder is buried in adhesions and firmly contracted on itself, or perhaps on one or more calculi. In such cases the wall of the gall-bladder is often almost inseparable from the calculi. If the calculus is a large one, the gall-bladder may be palpable as a tumour of stony hardness. The walls of the gall-bladder may undergo calcification, and cholesterin may be deposited in the tissues. When extensively calcified, the gall-bladder may be felt through the abdominal wall and will resemble a gall-bladder filled with a large gall-stone. Claude² found a calcified gall-bladder the size of a turkey's egg in a woman aged ninety-four.

Chronic ulcerative cholecystitis is usually, but not invariably, associated with calculi. In Norman Moore's³ case there were multiple ulcers but no real calculi, and in Locke's⁴ thirty ulcers without any gall-stones. The gall-bladder may shew pericholecystitic adhesions; I have seen the omentum completely rolled round the gall-bladder in a case in which a small gall-stone had worked its way through the gall-bladder wall and was adherent externally, the ulcerative passage having become obliterated. Chronic ulcerative cholecystitis may be latent until perforation and acute peritonitis occur.

Chronic Empyema of the Gall-bladder. (*Vide* p. 613.)

Tuberculosis.—Very few cases of tuberculous cholecystitis have been recorded; Simmonds⁵ describes two distinct forms: (i) Chronic ulcerative, of which Latronche⁶ collected 7 cases (Riedel, Czerny, Braquehay, Tédénat⁷ (3), and his own), all in women and all with gall-stones. The condition may be responsible for a persistent fistula after cholecystotomy. (ii) Acute tuberculosis with necrosis of the mucous membrane. Lancereaux⁸ reported tuberculosis of the gall-bladder, cystic and common bile-duets in a woman aged thirty-two years.

¹ Mayo. *Ann. Surg.*, 1899, xxx, 490.

² Claude, H. *Bull. Soc. Anat. Paris*, 1897, lxxii, 219.

³ Moore, N. *Trans. Path. Soc.*, Lond., 1891, xlii, 178.

⁴ Locke, E. A. *Boston Med. and Surg. Journ.*, 1906, cliv, 703.

⁵ Simmonds, M. *Centralbl. f. allg. Path. u. path. Anat.*, Jena, 1908, xix, 225 (Orig.).

⁶ Latronche. *Journ. de méd. de Bordeaux*, 1911, xli, 517.

⁷ Tédénat. *Rev. de chir.*, Paris, 1910, xlii, 1178.

⁸ Lancereaux. *Traité des maladies du foie et du pancréas*, p. 662, 1899.

Actinomycosis.—Mayo Robson¹ operated successfully on a case of this nature, which appears to be unique.

Syphilis.—Fowler² reported a rather doubtful case of syphilitic cholecystitis, the gall-bladder being much thickened and contracted.

PARASITIC AFFECTIONS OF THE GALL-BLADDER

Hydatid cysts hardly ever arise in the gall-bladder itself. Cases have been reported by Bowman,³ J. K. Thornton,⁴ F. Page,⁵ Langenbuch,⁶ Huber,⁷ and Barling and Burton,⁸ McGavin's⁹ specimen was removed from a woman aged thirty-two years during life, but the committee of the Pathological Society, on which I was, reported that the cystic tumour was not the gall-bladder, but a hydatid cyst which had arisen in its neighbourhood and probably displaced it. A number of cases described from clinical evidence, viz. jaundice, a distended gall-bladder, and disappearance of these signs after the passage of hydatid membranes by the bowel, as hydatid disease of the gall-bladder, are open to the criticism that they may have been examples of rupture of a hydatid cyst into the bile-ducts, with subsequent obstruction of the common bile-duct. Cysts have been found loose in the gall-bladder, but this does not prove that the gall-bladder was the primary site of the parasite (Reade¹⁰). It is conceivable that small daughter cysts which have entered the ducts from rupture of a cyst might pass up a cystic duct which had previously been dilated by a gall-stone, but it would hardly be possible for them to work their way up a normal cystic duct on account of the spiral valves of Heister. A hydatid cyst in the liver may, under conditions such as suppuration, discharge into the gall-bladder; and Bland-Sutton¹¹ operated upon a hydatid cyst of the omentum which opened into the gall-bladder. The symptoms of hydatids in the gall-bladder are much the same as those of rupture of a hydatid cyst into the bile-ducts.

Fasciola Hepatica.—Budd, in his book on Diseases of the Liver, mentions cases in which liver flukes have been found loose in the gall-bladder.

¹ Robson, Mayo. *Med.-Chir. Trans.*, Lond., 1905, lxxxviii, 225.

² Fowler. "Syphilis of the Gall-bladder and Bile-ducts," *New York State Journ. Med.*, 1908, viii, 540.

³ Bowman. *Lancet*, Lond., 1876, i, 532.

⁴ Thornton, J. K. *Ibid.*, 1891, i, 763.

⁵ Page, F. *Ibid.*, 1898, i, 995.

⁶ Langenbuch. *Deutsche med. Wchnschr.*, 1900, xxvi.

⁷ Huber. *Deutsches Arch. f. klin. Med.*, 1891, xlviii, 432. (Multilocular Hydatid.)

⁸ Barling and Burton. *Birmingham Med. Rev.*, 1897, xlii, 234.

⁹ McGavin. *Lancet*, Lond., 1902, i, 504; *Trans. Path. Soc.*, Lond., 1902, liii, 351.

¹⁰ Reade. *Lancet*, Lond., 1907, i, 882.

¹¹ Bland-Sutton. *Gall-stones and Diseases of the Bile-ducts*, p. 116, 1907.

STOMIARIS
common in
the bile ducts
the Japanese
and Chinese
may wonder
at it

DÉVE explains all the reported cases as due to
rupture of a deep-seated hydatid in the liver into
either the gall bladder or the ducts

^ Chauffard argues that hydatid embryos arriving by the portal vein may pass into the
cystic veins and so primarily infect the gall bladder

Ascaris lumbricoides. Although about 90 cases of invasion of the bile ducts have been
reported, there are not many examples of their presence in the gall bladder.
Aviles has collected about seven.

DÉVE, F. Compt. rend. Soc. Biol., Paris, 1921, LXXXV, 632

Chauffard. Ann. de méd., Paris, 1918, V, 561

AVILES. Surg., Gyn., and Obst., Chicago 1918, 459

Papillomas of the gall bladder may be divided into (1) the large and (2) the small

; Abell / x
In Abell's case the common
bile duct contained a similar
growth after operation removal
of one in the gall bladder. ^

Abell, I. Ann. Surg. Phila., 1923, LXXVIII, 276

INNOCENT TUMOURS OF THE GALL-BLADDER

INNOCENT tumours are rare in the gall-bladder, and are not nearly so often met with as malignant growths.

(1) A ^{large} papilloma of the mucous membrane of the gall-bladder is rather rare—far rarer than carcinoma. I have examined 3 cases. Zenker¹ suggested that papilloma is the early stage of carcinoma; this may be true for some cases of villous carcinoma, but it certainly does not hold good for all cases of carcinoma of the gall-bladder. If it were so, routine examination of the gall-bladder would shew that papillomas are comparatively common.

A papilloma is usually associated with gall-stones; in 8 cases collected by Sand and Mayer² calculi were present in 7. It might naturally be expected that the papilloma is secondary to the irritation of calculi; but a papilloma may occur in the absence of any evidence of cholelithiasis. It is possible that some cases regarded as villous carcinoma of the gall-bladder are really large innocent papillomas.

Chappet³ described a large villous cancer in the gall-bladder attached to the mucosa by two very thin pedicles in a man aged seventy-nine years; there was a calculus in the common bile-duct.

The papilloma is a soft wavy mass which is extremely friable and breaks up on examination so easily that it may, when removed at an operation, suggest material which would later form a gall-stone. After death it is deeply bile-stained. A papilloma may fill up the gall-bladder (Sand and Mayer); or it may become detached and lie loose in the gall-bladder. Microscopically there is a delicate papillomatous growth covered with columnar or subcolumnar cells. In specimens removed during life from the gall-bladder it is impossible, from microscopic examination, to say whether it is a simple papilloma or the superficial part of a villous carcinoma. The structure of the papilloma removed after death is difficult to make out in the microscopic sections I have seen, from the staining and degeneration due to soaking in the bile. A good microscopic drawing is given by Pals-Leusden.⁴ V. Schueppel⁵ examined microscopic sections of a myxomatous papilloma from a gall-bladder which did not contain any bile. When the papilloma becomes oedematous or undergoes mucoid degeneration, a succulent tumour (myxomatous papilloma) results. No clinical symptoms can be correlated with papilloma of the gall-bladder. The two following examples of

¹ Zenker. *Deutsches Arch. f. klin. Med.*, 1888-9, xliv, 159.

² Sand et Mayer. *Arch. de méd. expér. et d'anat. path.*, Paris, 1911, xxiii, 523.

³ Chappet. *Lyon méd.*, 1894, lxxvi, 146.

⁴ Pals-Leusden. *Arch. f. klin. Chir.*, 1906, lxxx, 128.

⁵ v. Schueppel. v. Ziemssen's *Cyclopaedia of Practical Medicine*, 1880, ix, 56.

papilloma of the gall-bladder have come under my notice at St. George's Hospital:—

A man aged forty-five died in St. George's with cardiac dilatation secondary to arteriosclerosis. The gall-bladder felt rather like a varicocele, and when opened contained a yellow, bile-stained, papillomatous mass growing from the anterior surface of the gall-bladder close to the fundus. The wall was not thickened or invaded. There were no calculi in the gall-bladder or bile-ducts, but the common duct was dilated, as if by the passage of calculi. In a man who died of pulmonary tuberculosis at the age of thirty-nine the gall-bladder contained a small bile-stained papilloma. There were no calculi in the gall-bladder or ducts, and no dilatation of the ducts. There had been no abdominal symptoms.

A submucous fibroma of the gall-bladder has been described.¹ A caution may be thrown out, however, not to regard the early stage of primary carcinoma of the gall-bladder as a fibroma.

Adenoma is extremely rare. It may be cystic.

Stanmore Bishop² removed a cystic tumour from the gall-bladder of a woman aged forty-two years who had had bilious attacks accompanied by transient jaundice. The tumour contained a number of separate cavities lined by cylindrical epithelium. I have examined a similar specimen from the fundus of the gall-bladder in a woman aged fifty-nine; there were no gall-stones. Terrier and Auvray³ quote a case of Wiedemann's; Mayo Robson⁴ records a case in which the loculi contained cholesterin. A *fibro-adenoma* at the fundus of the gall-bladder is figured by Moynihan⁵ from a specimen in the London Hospital Museum. Sutherland⁶ recorded a small *adenomyoma*.

Small cysts in the mucous membrane of the gall-bladder containing cholesterin are also ^{occasionally} rare. Terrier and Auvray refer to a case of Adler's in which a gall-bladder presented three such cysts. The cholesterin-containing cysts may develop into parietal calculi embedded in the wall of the gall-bladder. Hydatid cysts are referred to on p. 628.

Oedema under the peritoneal coat of the gall-bladder is sometimes seen in cases of backward pressure due to heart disease or chronic bronchitis and emphysema. When localised it may look like a small cyst; microscopically it is seen that there is no true cavity, and only oedema of the tissues.

Fatty Tumours.—Local subperitoneal masses of fat are in rare instances seen on the gall-bladder. I have seen this in otherwise perfectly normal gall-bladders. As a result of cholecystitis it is conceivable that an appendix epiploica might become adherent to the gall-bladder and subsequently be detached from the colon.

¹ Albers, quoted in v. Ziemssen's *Cyclopaedia of Practical Medicine*, 1880, ix, 567.

² Stanmore Bishop. *Lancet*, Lond., 1901, ii, 72.

³ Terrier et Auvray. *Chirurgie du foie*, p. 253, 1901.

⁴ Mayo Robson. *Med.-Chir. Trans.*, Lond., 1905, lxxxviii, 229.

⁵ Moynihan. *Gall-stones and their Surgical Treatment*, p. 135, 1906.

⁶ Sutherland. *Glasgow Med. Journ.*, 1898, i, 216.

(11) Small papillomas have been shown to be comparatively common; MacCarty found multiple papillomas twice to 6 times the length of the villi in 4 per cent of 5000 removed gall bladders; and among 288 cholecystectomies Abell found 5 adenomas and 3 papillary adenomas.

✓ According to Kaufmann it forms
5 per cent. of all cases of
carcinoma examined after death.

✓ The order of frequency with which the
organs of digestion are attacked by primary
malignant disease

Landsteiner recorded a myo-
sarcoma combined with
squamous called carcinoma | 1

Carson and Smith record
a round celled sarcoma
associated with gastro

Iwasaki's case.
quoted by Sweng

Kaufmann, Lehrbuch

Carson and Smith. Ann. Surg., 1915, LXII, 688.

Miller Root. med. and Surg. Journ., 1924, CXCII,
1074

PRIMARY MALIGNANT TUMOURS OF THE GALL-BLADDER

FRERICHS¹ gave an account of the disease in 1861; Villard,² in 1870, collected 17 cases; Musser,³ in 1889, 100 cases; Courvoisier,⁴ 103; and in 1901 Fütterer,⁵ 268. These tables, of course, deal largely with the same cases. The bibliographies attached to Siegert's,⁶ Ames's,⁷ and Fütterer's papers shew that the subject has no cause to complain of neglect. ~~This disease has certainly received more attention of late years;~~ of Fütterer's 268 cases, no less than 195 were reported since 1880.

It is remarkable that another annexe of the alimentary canal, the vermiform appendix, in which concretions are comparatively common, is much less often attacked by primary malignant disease. They are both frequently inflamed, and are both very liable to irritation, infection, and calculi.

Morbid Anatomy.—Primary malignant disease of the gall-bladder is practically always carcinoma. I have references to 14 cases of primary sarcoma.

Musser mentions 3 cases of primary sarcoma; Griffon and Segall⁸ record a spindle-celled sarcoma, primary in the gall-bladder, which contained two calculi, in a woman aged seventy-six. Czerny (angio-sarcoma), Riedel,⁹ Neviadomsky,¹⁰ Landsteiner,¹¹ Parlavecchio,¹² and Bayer¹³ (2) have also met with primary sarcoma of the gall-bladder. Becker¹⁴ described a primary endothelioma, and Bland-Sutton¹⁵ a perithelioma, of the gall-bladder; in Becker's case there were two gall-stones which had almost perforated into the stomach near the pylorus. Wieting and Hamdi¹⁶ described a primary malignant melanotic tumour (melanoblastoma) of the gall-bladder. The growth was a spindle-celled sarcoma in at least 4 cases (Griffon and Segall, Landsteiner, Bayer). I have examined 1 case of primary spindle-celled sarcoma of the gall-bladder. A woman aged fifty-six had a large tumour to the right of the umbilicus which entirely replaced the gall-bladder; it contained a cavity which opened into the transverse colon. The growth had tracked along the cystic and common bile-ducts and projected at the biliary papilla. No gall-stones were found. There were metastases in the aortic

¹ Frerichs. *Diseases of the Liver*, ii, 479. Transl. New Sydenham Soc., 1861.

² Villard. *Bull. Soc. Anat. Paris*, 1869, xlv, 217.

³ Musser, J. H. *Boston Med. and Surg. Journ.*, 1889, cxxi, 525.

⁴ Courvoisier. *Pathologie und Chirurgie der Gallenwege*, Leipzig, 1890.

⁵ Fütterer, G. *Über die Ätiologie des Carcinoms*, Wiesbaden, 1901.

⁶ Siegert. *Virchows Arch.*, 1893, cxxxii, 353.

⁷ Ames, D. *Johns Hopkins Hosp. Bull.*, 1894, v, 74.

⁸ Griffon et Segall. *Bull. Soc. Anat. Paris*, 1897, lxxii, 586.

⁹ Riedel. *Berlin. klin. Wehnschr.*, 1882.

¹⁰ Neviadomsky. *Med. Obozr.*, Mosk., 1900, liii, 190.

¹¹ Landsteiner. *Wien. klin. Wehnschr.*, 1904, xvii, 162, and *Bechr. f. Klin. Med.*, 1907, Lxii, 427

¹² Parlavecchio. *Arch. f. klin. Chir.*, Berlin, 1908, lxxxvii, 365.

¹³ Bayer. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1909, xlvi, 429.

¹⁴ Becker, W. *Journ. Am. Med. Assoc.*, 1903, xl, 903.

¹⁵ Bland-Sutton. *Lancet*, Lond., 1907, i, 1343.

¹⁶ Wieting und Hamdi. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1907, xlii, 23.

lymphatic glands and in a gland in the right groin. There was no jaundice. Microscopically it was a spindle-celled sarcoma, somewhat alveolar in arrangement, with numerous blood spaces. The patient was in St. George's Hospital in 1891.

The following description will deal with carcinoma of the gall-bladder.

Histology.—Carcinoma of the gall-bladder varies in the form of the cells and in their arrangement; it may be columnar- or spheroidal-celled. The cells may undergo colloid degeneration, or the cavities of the tubes lined by columnar epithelium may become distended by mucoid material

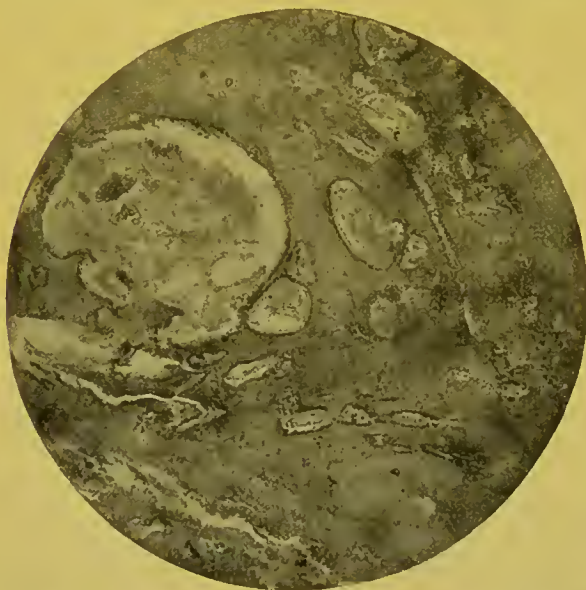


FIG. 86.—Microscopic appearances of columnar-celled carcinoma of the gall-bladder. Shews dilated spaces lined by columnar epithelium and containing mucus. (Photomicrograph by Dr. S. G. Penny.)

without any colloid degeneration of the cells (Fig. 86). Columnar-celled carcinoma may grow into the cavity of the gall-bladder as a villous tumour or papilloma; but the invasion of the deeper layers does not shew a papillomatous arrangement, and is an ordinary columnar-celled carcinoma with a fair amount of fibrous tissue. Frequently a change of type of the carcinoma is visible; parts of the growth may be columnar-, others cubical-, and other parts spheroidal-celled. This transition is seen in columnar-celled carcinoma elsewhere, especially in duct cancer of the breast. In transitional parts, and especially when colloid or allied degenerative changes are present, the large epithelial cells may be so far modified as to appear flattened.¹ Multinuclear cells are also sometimes seen. As the result of metaplasia a squamous-celled carcinoma of the gall-bladder may occur.

Deetz (*Virchows Arch.*, 1901, clxiv, 381) described 4 cases and Fütterer (*Journ. Amer. Med. Assoc.*, Chicago, 1904, xliii, 1129) collected 13 examples; to these the cases described by Hebb (*Westminster Hosp. Rep.*, 1895, ix, 316), Mayo Robson (*Med.-Chir. Trans.*, Lond., 1896, lxxix, 159), Speese (*Univ. Penn. med. Bull.*, 1904, xix, 300), Herxheimer, Nicholson (3) (*Journ. Path. and Bacteriol.*, 1909, xiii, 41), M'Kenzie (*ibid.*, 1909, xiii, 99), and one at St.

¹ For a discussion of this change see Bret. *Lyon méd.*, 1898, lxxxix, 41.

According to Nicholson a lining of
squamous epithelium has only once
been seen in the gall bladder,
namely by Lubarsch.

Nicholson. Guy's Hosp. Rep. 1918, LXIX, 211.
Lubarsch. Arch. a. d. path.-anat. hist. Pozn., Wiesbaden
1901, 205

George's Hospital, should be added, making 22 in all. Deetz, in an examination of 300 gall-bladders, including some with cholelithiasis, never observed transformation of the lining epithelium into squamous epithelium, but he nevertheless believes this change must occur to account for a primary squamous-celled carcinoma of the gall-bladder. λ

Besides the mucoid and colloid changes already mentioned, fatty and other degenerations of the cells may occur, and parts of the tumour

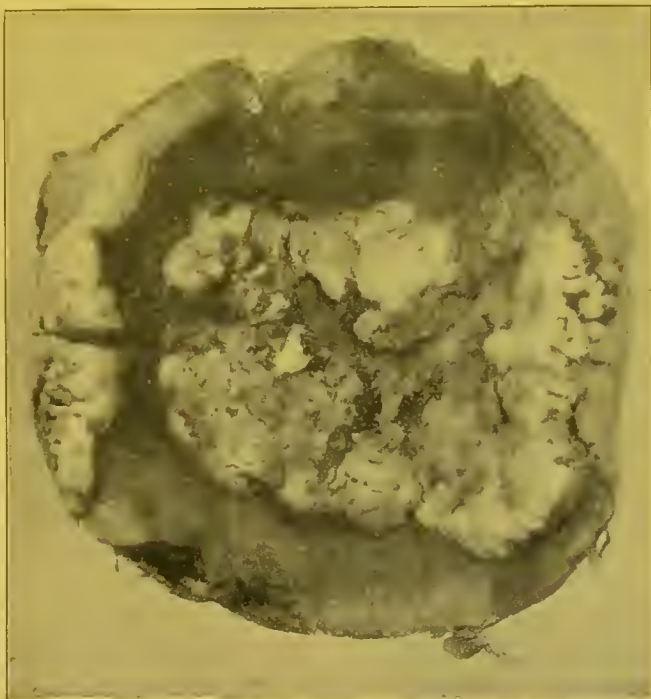


FIG. 87.—Squamous-celled carcinoma of the gall-bladder. Specimen (Series ix, 197D) in St. George's Hospital Museum. (Photograph by Dr. ~~R. B. Thorne~~)

λ B. S. TAYLOR

may become necrotic. Occasionally haemorrhages take place into the tumour.

Starting-point of the Growth.—It has been thought that spheroidal-celled carcinoma is derived from the mucous glands in the wall of the gall-bladder, and columnar-celled carcinoma from its lining mucous membrane. But the change from a columnar- to a spheroidal-celled carcinoma can be seen in the same specimen, and there is no essential difference between the columnar cells of the surface mucous membrane and of the mucous recesses or "glands" in communication with it. It may be concluded that carcinoma, whatever its form, arises from the mucous membrane as a whole, and no statement that either form of carcinoma arises exclusively from the surface epithelium of the gall-bladder or from the epithelium lining the "glands" is justified.

It has been suggested that carcinoma of the gall-bladder begins as

a papilloma.¹ Although this may be true in some instances, there is certainly no proof that it always holds good. Papilloma of the gall-bladder is rare. Moreover, some cases of carcinoma of the gall-bladder do not shew any villous projection into the lumen of the cavity, but are



FIG. 88.—Carcinoma in the position of the gall-bladder containing calculi. From a specimen (Series ix, No. 197E) in St. George's Hospital Museum.

limited to the infiltration of its wall. Chronic inflammatory changes in the gall-bladder, analogous to pre-cancerous mastitis, appear to play an important part in the development of carcinoma. In five gall-bladders presenting the appearances of universal chronic inflammatory thickening without any naked-eye evidence of growth, Slade² found carcinoma. Carcinoma of the gall-bladder may, like carcinoma of the intestine, occur in two forms: (1) That projecting into the cavity of the gall-bladder as a fungating growth; (2) that limited to infiltration of its walls. The fungating form is generally papilloma-

tous, and histologically a columnar-celled growth; the infiltrating form, though it may be columnar-celled, is often a spheroidal-celled carcinoma. The two forms may be combined.

Situation of the Tumour.—Carcinoma most commonly starts in the fundus, and the distal compartment of an hour-glass gall-bladder may be the starting-point of the growth. The explanation of this is that the fundus, being the most dependent part, is specially exposed to irritation by calculi. A growth midway between the fundus and the cystic duct may divide the gall-bladder into two compartments or produce an hour-glass gall-bladder (Fig. 89). The growth may begin at the neck of the

¹ Zenker, *Deutsches Arch. f. klin. Med.*, Leipz., 1889, xliv, 159; Aczel, *Virchows Arch.*, 1896, cxliv, 86; Warthin, *Phila. med. Journ.*, 1900, vi, 38.

² Slade. *Lancet*, Lond., 1905, i, 1059, and private communication.



gall-bladder, at its junction with the cystic duct, and then give rise to obstruction, either by blocking the lumen or by spreading around the circumference of the narrowed gall-bladder or cystic duct, and producing an annular stricture. As a result the gall-bladder may become distended with fluid. Carcinoma of the cystic duct is much the same as carcinoma of the neck of the gall-bladder, and clinically resembles that condition rather than carcinoma of the other bile-ducts. Carcinoma of the neck of the gall-bladder may appear to depend on the irritation of calculi impacted in that situation.

The growth may, however, involve the whole of the gall-bladder, so that it is difficult or impossible to say in what part—fundus, neck, etc.—it arose. In other cases the place of the gall-bladder is entirely taken by growth; and the condition may be erroneously regarded as primary (massive) carcinoma of the liver. That the growth originated in the gall-bladder is then assumed from the complete absence of that viscus, or from the presence of calculi embedded in the centre of a growth in the position of the gall-bladder (*vide* Fig. 88).

A secondary growth in the gall-bladder may, to the naked eye, resemble a primary neoplasm.

A specimen in St. Bartholomew's Hospital Museum (No. 2216G) looks like a primary tumour, but is really, as shewn by section of the walls of the gall-bladder, a nodule of round-celled sarcoma, secondary to a growth in the lung.

Behaviour and Appearance of the Tumour.—The columnar-celled form may project into the gall-bladder and fill it with a villous growth which easily disintegrates, and then somewhat resembles caseous pus or plaster-like material, imitating both in structure and in appearance psorospermiosis of the bile-ducts in a rabbit's liver. But a columnar-celled carcinoma of the gall-bladder may be hard and solid, and not the least villous in arrangement. So, as in the breast, a columnar-celled carcinoma may occur in one of two forms: (i) villous; (ii) like an ordinary columnar-celled carcinoma of the bowel. Generally speaking, the spheroidal-celled carcinoma grows more rapidly and generalises more freely. But the columnar-celled form may spread by continuity into the liver substance, and then shew a transition to the spheroidal-celled type.

Haemorrhage into the gall-bladder from a villous carcinoma is rather rare; it occurred 7 times in Musser's 100 cases. Colloid change is commoner in the more slowly-growing columnar-celled growths than in the spheroidal-celled carcinoma. Carcinoma in an early stage may appear as a localised thickening, like a button, of the wall of the gall-bladder, of a whitish appearance, and may resemble a scar or a gumma. As a rule the tumour is not larger than the closed fist; Michaux¹ records a tumour the size of an adult's head; it was diagnosed as an ovarian cyst.

Extension by Continuity.—As already mentioned, a large tumour in the gall-bladder may directly invade the liver, and thus give rise to consider-

¹ Michaux. *Bull. et mém. Soc. chir. de Paris*, 1907, xxxiii, 1182.

able hepatic enlargement. In these cases the growth may be thought to be a primary carcinoma of the liver.

In one case which I examined, the neoplasm spread from the anterior surface of the gall-bladder into the liver, and projected so little into the cavity of the gall-bladder that it was only on section that it became clear that the tumour started in the gall-bladder. In this instance the primary growth was confined to the surface of the gall-bladder in contact with the liver, and so might have been overlooked, and the numerous secondary growths in the liver might, therefore, have been regarded as multiple primary carcinoma.

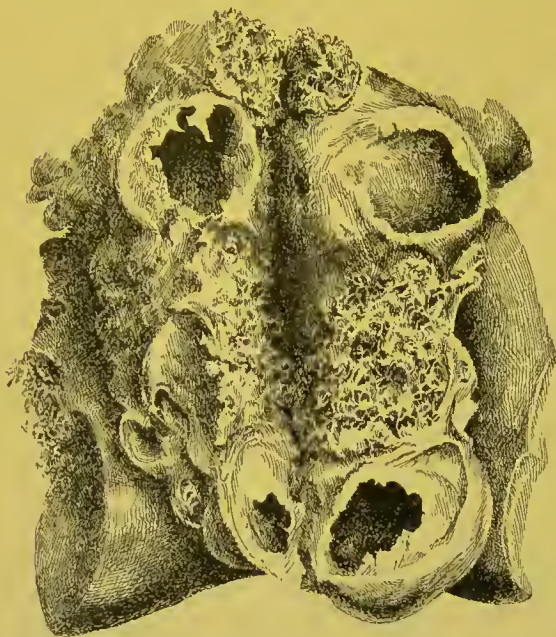


FIG. 89.—Papillomatous form of primary carcinoma of the gall-bladder. The gall-bladder has been opened longitudinally; the growth does not occupy the whole of the gall-bladder, the fundus and neck being unaffected. From a specimen (Series ix, 197A) in St. George's Hospital Museum. (Drawn by Dr. E. A. Wilson.)

growth started in the bile-ducts and then extended, or originated in the gall-bladder. Carcinoma of the gall-bladder has been known to project as a free process down the cystic duct into the common bile-duct (Bohnstedt¹), in the same manner that malignant disease of the liver has, in at least one case (Gilbert and Claude²), been found projecting into the extra-hepatic bile-ducts.

Fistulae.—When, as is usually the case, carcinoma begins in the fundus of the gall-bladder, it readily becomes adherent to the colon and may open into it. This occurred in 10 of Musser's 100 cases, and in 6 of Riedel's³ 77 cases. Perforation may occur into the stomach; this was noted in 5 of Riedel's cases. In like manner a carcinomatous gall-bladder may open into the duodenum; this occurred in 10 of Riedel's cases. But this fistula is less often seen in carcinoma than in chole-

¹ Bohnstedt, quoted by Devic et Gallavardin, *Rev. de méd.*, Paris, 1901, xxi, 569.

² Gilbert et Claude. *Arch. gen. de méd.*, Paris, 1895, clxxv, 513.

³ Riedel. *München. med. Wchnschr.*, 1911, lviii, 1337.



D. Symmers mentions direct
invasion of the right renal
vein by a carcinomatous
gall-bladder.

Symmers, D. Amer. Journ. Med. Sc., Phila., 1917, cliv,
225

lithiasis. The growth may invade the duodenum so widely that it may be difficult to decide in which situation it started.

Coupland¹ described a primary carcinoma of the first part of the duodenum, which grew into and entirely replaced the gall-bladder. Inasmuch as primary carcinoma is much rarer in the first part of the duodenum than in the gall-bladder, it is possible that the growth was primary in the gall-bladder.

The tumour has been known to invade the abdominal wall, then to set up an abscess, and even an external fistula.

In a woman, aged sixty years, who died in St. George's Hospital, carcinoma of the gall-bladder spread to the cystic duct and then ulcerated into the common bile-duct and portal vein; from this fistula extensive haemorrhage into the common duct and duodenum resulted. There was no clot in the portal vein.

Pressure Effects.—When the growth implicates the pylorus, it may cause obstruction, and clinically simulate carcinoma of the pylorus. From their anatomical relations this is more likely to occur when the growth is near the neck of the gall-bladder.

Rabé and Rey² found the fundus of a carcinomatous gall-bladder firmly adherent to the first part of the duodenum, which was greatly narrowed, and had led to dilatation of the stomach. The colon was also adherent to the gall-bladder, and the intestinal obstruction in the case was thus partly explained. Lejonne and Milanoff³ recorded a somewhat similar case.

Thrombosis of the portal vein may be associated with primary carcinoma of the gall-bladder; this occurred in 6 out of 68 cases of pylethrombosis collected by Lissauer.⁴

The gall-bladder may perforate into the peritoneal cavity, or give rise to a localised abscess (compare p. 644). Such a localised abscess may subsequently rupture into the general peritoneal cavity.

In a case reported by Moutier⁵ primary carcinoma of the gall-bladder opened into an encysted peritoneal pouch containing bile and imitating, both during life and at the necropsy, a dilated gall-bladder.

Secondary Growths.—The liver is the organ most frequently affected, being involved in about 50 per cent of the cases.

In Musser's⁶ 100 cases there were metastases in 55; the liver was involved in 52, the abdominal lymphatic glands in 16, the lungs or pleura in 10, and the peritoneum in 12.

When the growths are numerous, the clinical aspect of the case becomes that of malignant disease of the liver. Secondary growths in

¹ Coupland, S. *Trans. Path. Soc.*, Lond., 1873, xxiv, 103.

² Rabé et Rey. *Bull. Soc. Anat. Paris*, 1897, lxxii, 881.

³ Lejonne et Milanoff. *Ibid.*, 1900, lxxv, 133.

⁴ Lissauer. *Virchows Arch.*, 1908, cxcii, 278.

⁵ Moutier. *Arch. gén. de méd.*, Paris, 1905, clxiv, 2001.

⁶ Musser. *Boston Med. and Surg. Journ.*, 1889, cxxi, 528.

the portal lymphatic glands may compress the bile-ducts and portal vein, thus setting up jaundice and ascites. Metastases may occur in other abdominal lymphatic glands, in the peritoneum, the ovaries, and the lungs. Infection may travel into the chest along the lymphatic vessels, which pass immediately behind the sternum to the glands in the anterior mediastinum. A tumour may thus project from the chest even before the primary growth has been detected.

Beadles¹ described a case of primary carcinoma of the gall-bladder with a secondary growth as large as a cocoanut near the second rib on the right side. In S. West's² case the symptoms were those of mediastinal tumour, which the necropsy shewed to be secondary to a growth in the gall-bladder.

In rare instances the lymphatic glands above the clavicle may be enlarged and readily palpable during life. To this phenomenon the term "Virchow's gland" has been applied. In cases in which acute cholecystitis supervenes in a carcinomatous gall-bladder enlargement of lymphatic glands in the neighbourhood may be inflammatory and not necessarily malignant.

The liver may be healthy, but usually it is enlarged, either from distension with bile or from secondary growths. In some cases the growth extends directly into the substance of the right lobe, and, as pointed out elsewhere, the tumour may resemble a primary massive carcinoma of the liver. From infection of the bile-ducts suppurative cholangitis may occur and give rise to miliary abscesses in the liver. Of 60 cases tabulated by Winton³ 4 shewed miliary abscesses. Rupture of a suppurating bile-duct may give rise to an abscess in the immediate neighbourhood of the liver.

A woman, aged fifty, died under my care with jaundice of two months' duration, fever of a month's duration, and a hard tumour in the position of the gall-bladder. There was primary spheroidal-celled carcinoma of the gall-bladder, secondary growths in the portal glands, liver, and around the pancreas. The intrahepatic ducts were dilated and full of pus, and there was a large abscess under the right lobe of the liver. There was a contracting sinus in the first part of the duodenum which was stenosed and firmly adherent to the gall-bladder. The history was compatible with the view that a gall-stone had ulcerated out of the gall-bladder into the duodenum four years before. At the necropsy there were no calculi in the gall-bladder.

The *pancreas* may shew chronic inflammation due to the previous passage of calculi.

Etiology.—*Relation of Primary Carcinoma of the Gall-bladder and Gall-stones.*—Special interest attaches to the association of gall-stones and carcinoma of the gall-bladder, inasmuch as the calculi are generally thought to be the cause, whether by direct irritation or otherwise, of the neoplasm. Calculi are extremely common in primary carcinoma of

¹ Beadles, C. F. *Trans. Path. Soc.*, Lond., 1897, xlviii, 119.

² West, S. *Ibid.*, 1886, xxxvii, 144.

³ Winton, W. B. Unpublished Thesis for M.D. Cantab., 1902.



Carcinoma may supervene
years after calculi have
been removed by
operation, and even in
the scar of a cholecystotomy
(Schnabel)

Schnabel Amer. Journ. med. Sc., 1924, CLXI, 95

Fawcett and Rippmann. Fig. Guy's Hosp. Rep.,
1913, LXVII, 41

the gall-bladder. In Musser's 100 cases they were present in 69, and in only three instances was cholelithiasis definitely stated to be absent. Fütterer¹ and Habersfeld² estimated that calculi were present in 70 per cent; Winton in 81 per cent; Zenker³ in 85 per cent; Courvoisier⁴ in 91 per cent; Siegert in 95 per cent. Janowski⁵ in 40 cases of malignant disease of the gall-bladder records calculi in all. Possibly in some cases in which calculi are not present at the necropsy, they have been passed at an earlier stage; the case quoted above suggests that this may occur. Conversely, primary carcinoma of the gall-bladder occurs in from 4 to 14 per cent of all cases of cholelithiasis.

Schröder⁶ estimated that 14 per cent of persons with cholelithiasis eventually became the subjects of carcinoma of the gall-bladder; in 141 cases of gall-stones there were 20 of primary carcinoma. In ~~223~~ cases of gall-stones abstracted from 4/592 the post-mortem records of Guy's Hospital by Tieshurst⁷ there were ~~4~~ cases of carcinoma of the gall-bladder or cystic duct, or ~~12.3~~ per cent. Riedel⁸ estimated the percentage of primary carcinoma in cholelithiasis at from 7 to 8. 300 Among 268 cases of gall-stones at St. George's Hospital there were 11 cases of 3 primary carcinoma of the gall-bladder, or 4.1 per cent; this low percentage is possibly accounted for by the fact that in many instances minute bilirubin-calcium calculi were the only ones present. In 17 gall-bladders shewing chronic inflammatory or other changes associated with gall-stones, and in all but one instance from cases dying from the effects of gall-stones, Slade⁹ found carcinoma in 10, or 59 per cent; in 5 of these the condition was only detected microscopically. This is a startling and unusual experience. Among 315 cases of gall-stones in the insane, Candler¹⁰ found 2 cases only of primary carcinoma of the gall-bladder; he considers that hospital statistics shew an unduly high percentage of carcinoma because patients are admitted for that disease. In 24 cases of primary carcinoma of the gall-bladder at St. George's Hospital, 18, or 75 per cent, were associated with gall-stones. 24 30

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It has, however, been suggested that the calculi are secondary to the growth, and are the result of obstruction to the passage of bile or of other changes set up by carcinoma in the gall-bladder. If calculi were the result of obstruction pure and simple, they would be found more frequently in carcinoma of the bile-ducts, in which biliary obstruction is more constant and prolonged than in malignant disease of the gall-bladder. But they are less frequent, being present in 23 out of my 67 cases, while in carcinoma of the gall-bladder the percentage is about 90. Besides directly obstructing the exit of bile and mucus from the gall-bladder, a tumour in its wall might interfere with its contractions. Both these

¹ Fütterer, G. *Über die Ätiologie des Carcinoms*, Wiesbaden, 1901.

² Habersfeld. *Ztschr. f. Krebsforsch.*, Berlin, 1908, vii, 190.

³ Zenker, H. *Deutsches Arch. f. klin. Med.*, 1888-89, xlv, 159.

⁴ Courvoisier. *Path. u. Chirurg. der Gallenwege*, 1890.

⁵ Janowski. *Beitr. z. path. Anat. u. z. allg. Path.*, Jena, 1891, x, 449.

⁶ Schröder. Quoted by Naunyn, *Cholelithiasis*. Transl. New Sydenham Soc., 1896.

⁷ Tieshurst. Quoted by Hale White, *Clin. Journ.*, Lond., 1907, xxx, 275.

⁸ Riedel. *Berlin. klin. Wchnschr.*, 1901, xxxviii, 1.

⁹ Slade. *Lancet*, Lond., 1905, i, 1059.

¹⁰ Candler. *Proc. Roy. Soc. Med.*, 1911, iv (Path. Sect.), 87.

conditions would cause biliary stagnation and so favour infection, cholecystitis, and the production of calculi. Further, it is conceivable that the presence of a growth or its disintegration might modify the secretion from the mucous membrane of the gall-bladder. In this connexion it is important to bear in mind that the cholesterin in the bile is largely derived from the mucosa of the gall-bladder. Siegert¹ tried to settle the question whether the presence of a growth in the gall-bladder gave rise to the formation of calculi, by a comparison of the incidence of calculi in primary and in secondary carcinoma of that viscus. In 99 cases of primary disease calculi were present in 94; whereas in 13 cases of secondary growths in its walls they were present in only 2. In 25 other cases of secondary growths that I have collected or seen, calculi were present in one; so in these 32 cases of secondary growths in the gall-bladder gall-stones occurred in 3, or 9.4 per cent, or well within the limits, 5 to 12 per cent (Schröder²), of the incidence of gall-stones in routine post-mortem work. These figures, as far as they go, do not support the view that a growth in the gall-bladder is a factor of any importance in the production of gall-stones. It must, however, be admitted that the presence of a secondary growth in the gall-bladder is not quite the same as a primary tumour, especially as regards its relation to the mucous membrane. Metastases usually start under the serous coat, and need not invade the mucous coat, which produces cholesterin, whereas a primary carcinoma is due to changes in the mucous membrane.

There is undoubtedly a very definite relation between cholelithiasis and primary carcinoma of the gall-bladder. But gall-stones are so commonly present without carcinoma that some additional factor would seem to be necessary. Rough calculi would be more prone than smooth ones to irritate and set up proliferation of walls of the gall-bladder. ^g Possibly the part played by calculi is that of preparing the soil for the direct cause, whatever it may be, of carcinoma. ^g Gall-stones dispose to fresh attacks of cholecystitis, and in this way a pre-cancerous condition of the gall-bladder may result. The walls of a carcinomatous gall-bladder may shew chronic inflammation, and even calcareous infiltration.³ On the other hand, gall-stones are due to catarrh of the mucous membrane of the gall-bladder, and it might be suggested that carcinoma and gall-stones are both the results of forms of irritation which have much in common.

To sum up, gall-stones are present in the great majority of cases of primary malignant disease of the gall-bladder, whereas carcinoma occurs in from 14 to 4 per cent of cases of cholelithiasis. It appears that cholelithiasis is the earlier of the two conditions, and that carcinoma *per se*, whether local in the gall-bladder or present elsewhere in the body (*vide* p. 719), does not set up cholelithiasis.

In connexion with the close association between carcinoma of the gall-

¹ Siegert. *Virchows Arch.*, 1893, cxxxii, 353.

² Schröder. Quoted by Naunyn, who accepts this estimate, *On Cholelithiasis*, p. 38. Translated by New Sydenham Soc., 1896.

³ Beadles, C. F. *Trans. Path. Soc.*, Lond., 1896, xlvii, 69.

According to Lazarus-Barlow gallstones associated with primary carcinoma of the gall-bladder always contain relatively large amounts of radium, whereas gallstones without gall bladder carcinoma do not. Leitch's experiments with guinea-pigs point to the mechanical factor as solely responsible for carcinoma in a gall-bladder containing calculi, for pebbles produced carcinoma as readily as gallstones.

But that some individuals are more prone than others to develop carcinoma as the result of irritation.

Lazarus-Barlow, W.-O. Brit. med. Journ., 1914, i, 1002.

LEITCH, A. Brit. med. Journ., 1924, ii, 451

bladder and cholelithiasis the question of a similar association between renal calculi and tumours of the pelvis of the kidney is of interest. It must be remembered that both renal calculi and new growths of the renal pelvis are less common than gall-stones and carcinoma of the gall-bladder.

Kelynack¹ collected 23 examples of associated renal calculus and malignant renal tumours of various kinds. In 8 cases of papilloma of the pelvis of the kidney collected by Drew² calculi were present in 4. It is reasonable to suppose that the irritation of a calculus would give rise to a villous growth of the renal pelvis more readily than to malignant disease of the substance of the kidney.

Sex.—Malignant disease of the gall-bladder is much commoner in women. According to Fütterer's figures (202 females, 52 males), it is four times more often seen in the female sex. Musser's cases included 75 females and 23 males (or 3 to 1); Siegert's, 79 females and 14 males ($5\frac{1}{2}$ to 1); Ames gives the proportion of females to males as 4 to 1; Courvoisier, as 5 to 1. In 50 cases of Terrier and Auvray,³ 40 were women and 10 men. In Winton's 60 cases 43 were females and 17 males (5 to 2). This predominance of females in carcinoma of the gall-bladder corresponds to their greater liability to gall-stones, which is calculated by Schröder in the proportion of 5 to 1, by Murchison and Bouchard 3 to 2, and by myself as 4 to 3 (*vide* p. 723). The overwhelming majority of female patients among the subjects of gall-bladder carcinoma contrasts with the sex incidence in carcinoma of the bile-ducts; thus in 18 cases Musser found the sexes equally represented, and in my 85 cases 50 were males and 35 females.

The pressure of the corset on the liver may, as suggested by Fütterer,⁴ increase the friction between calculi and the walls of the gall-bladder, and so may help to explain the great predominance of females in primary carcinoma of the gall-bladder. In this connexion it is remarkable that the bile-ducts, which can hardly be affected in the same way by the wearing of a corset or belt, are more often the site of carcinoma in men than in women. Graham recorded carcinoma of the gall-bladder in a shoemaker whose last pressed upon the liver much as a corset might do, and Fütterer is inclined to think that pressure of this kind may be a factor in the male cases.

While primary carcinoma is much commoner in women, Siegert's statistics of secondary growths in the gall-bladder, though only 13, shewed that the male sex were affected in 10, or 77 per cent, and the female sex in 3, or 23 per cent.

Age.—Friedrichs described the disease as one of old age. In 17 cases collected by Villard 9 were over seventy years of age. The average age of Fütterer's large series was fifty-eight years, and was the same in 60

¹ Kelynack, T. N. *Renal Growths*, p. 27, 1898, Edin.

² Drew, D. *Trans. Path. Soc.*, Lond., 1897, xlviii, 133.

³ Terrier et Auvray. *Rev. de chir.*, Paris, 1900, xxi, 143.

⁴ Fütterer, G. *Chicago Med. Recorder*, 1897, xii, 325.

cases collected by Winton, many of them from the unpublished records of St. George's and other hospitals. It is very rare before forty years of age. Haas¹ and Chavannaz² have described cases in women of twenty-five years. At the other extreme the most advanced age was ninety (Thomas and Noica³). The average age of carcinoma of the gall-bladder in the two sexes was almost identical in Fütterer's 194 female and 45 male cases.

Clinical Picture.—The clinical manifestations are roughly divisible into three groups: (i) Symptoms connected with pre-existing cholelithiasis; (ii) the local effects of malignant disease of the gall-bladder; (iii) complications due to invasion of adjacent parts by the tumour and to metastases in the liver, peritoneum, and elsewhere.

The patient, generally a woman between fifty and sixty years of age, may have suffered from symptoms of gall-stones. Biliary colic may closely precede the development of carcinoma, but in some instances there is a very long interval between the first appearance of colic and the development of carcinoma.

Jourdan⁴ recorded a case in which the colic began twenty-five years before the growth appeared. Bret⁵ describes the case of a woman, who died at the age of thirty-six with carcinoma of the gall-bladder enclosing an oval calculus; she had had biliary colic since the age of twenty.

There is often, however, no history of gall-stone colic in fatal cases of carcinoma of the gall-bladder; the calculi may remain latent in the gall-bladder and never pass into the ducts. Kehr⁶ ~~says~~ that clinical evidence of cholelithiasis is wanting in the majority of the patients. In other instances pain really due to inflammation or adhesions around the gall-bladder is regarded as dyspepsia.

Usually the first thing noticed by the patient is a feeling of discomfort and heaviness in the right hypochondrium and parts around. According to Head,⁷ the eighth dorsal segment is the visceral area of cutaneous tenderness in connexion with the gall-bladder. There may be loss of appetite, gastro-intestinal disturbance accompanied by definite pain, and even attacks of colic, indistinguishable from biliary paroxysms. A tumour may be felt ~~in more than half the cases~~ in the situation of the gall-bladder, which is at first smooth and oval, and subsequently becomes hard, irregular, and may be tender. Like the liver, it moves with respiration unless fixed by adhesions. It may reach the size of a cocoanut. These may be called the local manifestations, and, on the whole, resemble those of cholelithiasis. As time goes on the growth invades neighbouring parts, and metastases may spring up; additional, or what may be called secondary, symptoms, are thus produced.

¹ Haas. *Prag. Vrtljhrshr.*, 1876, cxxxii, 31. Quoted by Fütterer.

² Chavannaz. *Gaz. hebdom. de méd.*, Paris, 1901, N.S., vi, 721.

³ Thomas et Noica. *Bull. Soc. Anat. Paris*, 1896, lxxi, 471.

⁴ Jourdan. *Ibid.*, 1891, lxvi, 323.

⁵ Bret. *Lyon méd.*, 1898, lxxxix, 35.

⁶ Kehr. *Diagnosis of Gall-stone Disease*, p. 92, 1901, American translation.

⁷ Head, H. *Brain*, Lond., 1893, xvi, 75.

and Fawcett and Ruppmann find

← this is important, for it ~~falls~~ ^{invalidates} that the argument that carcinoma
may supervene if operation is not undertaken in a case of
Cholelithiasis

Fawcett and Ruppmann. Gay's Hep. Rep., 1913, LXVII, 41

(but in 12 it was due
to calculi in the hepatic
or common bile ducts),

Carcinoma of the gall-bladder may remain latent and the symptoms may be entirely due to secondary growths (*vide* also p. 637).

A man aged sixty-eight in St. George's Hospital with ascites, but no jaundice, was diagnosed as cirrhosis. At the necropsy there was a primary columnar-celled carcinoma of the gall-bladder which contained gall-stones. The liver was directly invaded by the tumour, and there was a large, broken-down growth in the glands behind the pancreas, which compressed the portal vein. In a case in St. George's Hospital a secondary growth in the spine at first imitated caries. In a case of primary carcinoma of the gall-bladder a secondary growth in the right breast was naturally thought to be primary (Osler¹).

When the liver becomes infiltrated with secondary growths, the clinical aspect of the case may be that of carcinoma of the liver. Enlargement of the liver can be made out in about half the cases, but it may be obscured by ascites or by flatulent distension. The surface may be smooth when the enlargement is due to distension with bile, nodular from secondary growths, or there may be a definite tumour formed by the cancerous gall-bladder and the adjacent liver substance infiltrated by growth. The bile-ducts may also be invaded by direct extension of the growth or be compressed by secondary growths or by enlarged glands either in the portal fissure or in the neighbourhood of the pancreas. Jaundice is thus set up, and the symptoms are much the same as those of primary carcinoma of the head of the pancreas or of the bile-ducts. Though not a necessary result of carcinoma of the gall-bladder, jaundice is very frequent. In 30 cases collected by Meunier it was absent in only 4. ~~Permanent~~ jaundice occurred in ~~23~~ ~~over 50~~ per cent, of ~~23~~ ~~cases~~ ~~and~~ in 69 of Musser's 100 cases.

Fauscett
and Rippmann's

1/57 60

As Mayo Robson² points out, jaundice may be due to catarrh of the ducts, but in that event it would not be progressive as in malignant disease, but would vary or even pass away. I have seen several cases of carcinoma of the gall-bladder in which jaundice came on after vomiting and diarrhoea, as in catarrhal jaundice, but persisted until death, and at the necropsy was found to depend on definite obstruction to the ducts. ~~Jaundice may also be due to a gall stone in the common duct.~~

Warthin³ described a case of carcinoma of the gall-bladder in which jaundice, leucoderma, and pigmentation, suggesting Addison's disease, were present. After death secondary growths were found in both adrenals.

Ascites occurs in about one-quarter of the cases. In Winton's 60 cases it was present in 14. It depends not on malignant disease of the gall-bladder itself, but on complications set up by metastases or by extension of the primary growth. It may be associated with, but does not necessarily follow, pressure on the portal vein; but it is most satisfactorily explained by chronic peritonitis set up by secondary growths

¹ Osler. *Brit. Med. Journ.*, 1906, i, 2.

² Mayo Robson. *Brit. Med. Journ.*, 1897, i, 710.

³ Warthin. *Phila. Med. Journ.*, 1900, vi, 38.

on the peritoneum. When there are numerous peritoneal metastases, the effusion may be fatty as the result of cellular degeneration (chyliform or fatty ascites).

Oedema of the legs may occur in the late stages of cachexia, and be due to cardiac debility, or possibly to the pressure exerted on the inferior vena cava by a large ascitic effusion or by enlarged glands in the neighbourhood. Thrombosis of the inferior vena cava has been recorded. There is often dyspepsia, which in a few instances is due to pyloric obstruction due to direct invasion by the growth, and may then be associated with a dilated stomach. There may be vomiting, tympanites, and usually constipation, which may alternate with diarrhoea. Extension of the growth to the colon may give rise to chronic or eventually to complete intestinal obstruction. When deep jaundice has developed, the patient gradually passes into the condition of cholaemia. The temperature is normal or subnormal unless there are complications. Muscular wasting and loss of strength steadily progress, and eventually emaciation, exhaustion, and cachexia become extreme; the biliary toxaemia gives rise to haemorrhages, petechiae, epistaxis, and occasionally haematemesis and melaena, mental failure, delirium, coma, and death. Terminal infections may carry the patient off, and this without the temperature being necessarily raised.

Complications.—In rare instances the gall-bladder perforates into the peritoneal cavity and sets up peritonitis. Rixford¹ met with a case in which extensive haemorrhage so distended a carcinomatous gall-bladder that rupture occurred. The growth may perforate into the transverse colon, and, as a result, the gall-bladder may be infected and an abscess, either in the gall-bladder or in its immediate neighbourhood, may result.² Suppurative cholangitis may arise and spread into the liver, the gall-bladder or Wirsung's duct, and in the latter event set up acute suppurative pancreatitis. Pus may collect in the gall-bladder, either when the growth is in a very early stage, or when there are numerous metastases.

In a man aged fifty-two, whom I examined after death at St. George's Hospital, a primary carcinoma of the gall-bladder gave rise to numerous secondary growths in the liver, which, with the stomach, weighed 15 pounds. There were calculi and pus in the gall-bladder, and chyliform (fatty) effusions in the left pleura and the peritoneum.

A local peritoneal abscess may form close to a carcinomatous gall-bladder, or there may be circumscribed acute peritonitis in its neighbourhood.

This was present in a woman aged forty-five years upon whom exploratory laparotomy was performed for a large tumour in the hepatic region. A quantity of fibrin was found around a carcinomatous mass, in the position of the gall-bladder, enclosing two calculi.

¹ Rixford. *Trans. Am. Surg. Assoc.*, 1905, xxiii, 219.

² Blanc et Leray. *Bull. Soc. Anat. Paris*, 1897, lxxii, 69.

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is very difficult; in 48 cases
at Guy's hospital no correct
diagnosis was made (Fawcett
and Rippmann).

When cholecystitis supervenes in a carcinomatous gall-bladder micro-organisms may be absorbed and infect other parts of the body. Lorrain¹ reported a case of lithiasis and carcinoma of the gall-bladder, with cholecystitis and endocarditis. Pyloric obstruction and obstruction of the transverse colon due to direct extension of growth have been already referred to. Portal thrombosis may occur (*vide* p. 637).

Duration.—It is difficult to determine the duration of the disease, since the early symptoms so closely resemble cholelithiasis, with which it is almost always combined. Probably it remains latent for a considerable time, but when jaundice and cholaemia have set in, the end is near. Some cases die very soon after the onset of definite symptoms. On the whole, the average duration of the disease may be put down as less than six months.

Diagnosis.—The presence of a hard, nodular, progressively increasing tumour in the position of the gall-bladder in a patient about the age of fifty years, especially in a woman, suggests the disease. Dull pain, loss of appetite, and wasting are in favour of growth. The distinct shadow cast by x-rays has been found of diagnostic value by Goldmann.² When metastases can be felt in the liver or in the supraclavicular fossae, the diagnosis is practically clinched. The only fallacy is, of course, that there is a primary tumour somewhere else which has given rise to generalisation, and that among other places a secondary growth has developed in or close to the gall-bladder. Careful search for a primary neoplasm in the stomach, rectum, oesophagus, breast, and uterus should, therefore, always be made. Jaundice is not an early or essential symptom.

Differential Diagnosis.—*Gall-stones.*—Malignant disease, especially in the earlier stages when the growth is confined to the gall-bladder, is very like cholelithiasis, and since carcinoma in the vast majority of the cases develops subsequently to gall-stones, it is very difficult to say when malignant disease has begun. Enlargement of the gall-bladder is in favour of tumour, especially if it is progressive and nodular. On the other hand, extensive inflammatory thickening of the walls of the gall-bladder may closely simulate carcinoma, even when the parts are exposed during laparotomy, and this impression may be supported when the thick-walled viscus is punctured. An inflamed gall-bladder may clinically appear of stony hardness either from contained calculi, or, more rarely, from calcification of its walls. In addition, the occurrence of dense adhesions to the surrounding parts—colon, stomach, omentum, etc.—and inflammatory enlargement of glands in the portal fissure, lesser omentum, and around the common bile-duct, where it passes into relation with the pancreas, may all suggest, even when the abdomen is opened, that there is malignant disease either of the gall-bladder, pylorus, or colon, and that secondary growths in the glands, by pressure on the ducts, have given rise to jaundice. Gall-stones in the common duct may feel like glands invaded by carcinoma. In any doubtful case the gall-bladder should be

¹ Lorrain. *Bull. Soc. Anat.*, 1903, lxxviii, 527.

² Goldmann. *Proc. Roy. Soc. Med.*, Lond., 1908, i (Surg. Sect.), 17.

~ / should

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opened and not merely punctured. As time goes on the cachexia, increasing jaundice, and, most positive evidence of all, secondary growths, may appear and strengthen or decide the diagnosis.

Malignant Disease of the Liver.—In the later stages, when the liver is enlarged and presents either a large tumour or several small ones, the diagnosis from primary or secondary malignant disease is often very difficult or even impossible. The history of gall-stones would suggest that the primary growth might have started in the gall-bladder, and the original appearance of a tumour in that situation would strengthen the diagnosis in the absence of evidence pointing to primary carcinoma of the stomach, colon, or other parts. Unfortunately, a history of gall-stones is often absent, and a tumour in the position of the gall-bladder is felt in about half the cases only.

Syphilitic disease of the liver in rare instances imitates carcinoma of the gall-bladder. From cicatricial contraction and deformity a piece of the right lobe may become elongated and hard and be thought during life to be a carcinomatous gall-bladder (Gerhardt¹). In such cases the effect of antisyphilitic treatment must be the guide as to the diagnosis.

Carcinoma of the Stomach.—When the cancerous gall-bladder causes pyloric obstruction, it may naturally be regarded as carcinoma of the pylorus. There is an absence of the movable pyloric tumour, but, unfortunately, this may also occur in pyloric cancer. The history of gall-stones and the presence of jaundice point to a biliary origin for the gastric symptoms. A bismuth meal and examination with x-rays may give valuable help.

Carcinoma of the transverse colon in the neighbourhood may closely resemble carcinoma of the gall-bladder.

Carcinoma of the bile-ducts and of the head of the pancreas may be simulated by those cases of gall-bladder carcinoma in which jaundice occurs early. In the former conditions the gall-bladder is more often distended and smooth, whereas in the latter the tumour is hard, solid, and may be irregular, and the liver is more likely to be enlarged and shew secondary growths. The question of diagnosis between these two conditions is discussed on page 699. In malignant disease of the pancreas a tumour may sometimes be felt deep in the abdomen and close to the spine.

Tumours arising from the parts around the gall-bladder, such as a hydatid cyst, a floating kidney or renal tumour on the right side, or more rarely a tumour of the right suprarenal, may imitate carcinoma of the gall-bladder; or one of these conditions may be diagnosed when the growth is really in the gall-bladder.

In a man aged seventy-nine years who presented a rounded, tender lump the size of an apple in the right hypochondrium, without jaundice or ascites, the diagnosis lay between a calcified hydatid cyst and carcinoma of the gall-

¹ Gerhardt. *Semaine méd.*, Paris, 1898, xviii, 273.



bladder. At the necropsy there was carcinoma of the gall-bladder with miliary abscesses in the liver.¹

When a *floating kidney* gives rise to jaundice by traction or pressure on the bile-ducts, the clinical aspect may resemble that of malignant disease of the gall-bladder. The free mobility of a floating kidney and the fact that it can be displaced from continuity with the liver should prevent confusion with malignant disease of the gall-bladder. The lumbar region should be carefully examined, and the abdomen should be palpated in the knee-and-elbow position.

Under certain conditions *faecal accumulation* in the transverse colon may, by the colicky pains and the presence of numerous hard masses in the neighbourhood of the gall-bladder, suggest carcinoma of the gall-bladder with secondary growths around. Examination under an anaesthetic may shew that these masses can be indented by the finger, and subsequent investigation that they vary in position and in number. In such cases the effect of purgatives and massage should be tried.

The **prognosis and treatment** may be considered (1) from a medical, and (2) from a surgical point of view.

(1) The disease being necessarily fatal unless it can be removed, medical treatment is merely palliative, and consists in the relief of pain and discomfort by morphine and opium, of vomiting and nausea by bismuth, hydrocyanic acid and morphine, and of constipation and intestinal fermentation by diet, calomel, salol, or various antiseptic remedies. Under such treatment the prognosis is of the gloomiest.

(2) If the growth be removed and there are no metastases, the prognosis should be more hopeful.

Quénu² collected 93 cases of cholecystectomy for carcinoma with an operative mortality of 18 per cent; out of 52 cases in which information was obtained, 14 were alive a year after operation, but only 5 or 6 were really satisfactory. The high mortality from operation mainly depends on haemorrhage; thus, there may be constant oozing from the wound, and after death extensive haemorrhagic infiltration around the ducts and pancreas. This tendency to haemorrhage should always be guarded against by giving large doses of calcium salts to jaundiced patients before operation. Calcium salts do not always prevent haemorrhage in jaundiced patients, and it is possible that degeneration of the vessel-walls is responsible for the haemorrhagic tendency, either alone or in addition to diminished coagulation power of the blood (Berg³).

After recovery from operation a biliary fistula is sometimes left. In some instances there is temporary improvement after resection of the gall-bladder, but nearly all cases shew a recurrence, often within six months. The following case illustrates the extreme malignancy of primary carcinoma of the gall-bladder, even when removed in a very early stage and apparently under the most favourable conditions.

¹ Lejonne et Malanoff. *Bull. Soc. Anat. Paris*, 1900, lxxv, 133.

² Quénu. *Rev. de chir.*, Paris, 1909, xxxix, 245.

³ Berg. *Ann. Surg.*, 1903, xxxviii, 356.

Heidenhain,¹ in the course of an operation on the gall-bladder for the removal of six calculi, noticed a small, button-like thickening in its wall and removed the gall-bladder; microscopically it was carcinomatous. Three months later the patient died from growths in the liver, though at the operation it appeared perfectly healthy.

The success of the operation depends on its early performance and on the absence of secondary growths, and this cannot be excluded before laparotomy. The diagnosis being difficult, cases occur in which laparotomy is undertaken with a view of relieving cholelithiasis, and carcinoma of the gall-bladder is found, perhaps in an early stage. Such early cases are the most favourable for cholecystectomy.

According to Carl Beck,² 40 per cent of the cases operated upon for cholelithiasis have carcinoma of the gall-bladder.

SECONDARY MALIGNANT TUMOURS in the gall-bladder sometimes occur in widespread carcinoma or more rarely sarcoma. The growths are usually either on the peritoneum, as in cases of extensive malignant disease of the peritoneum, or just under the peritoneal covering of the gall-bladder. The growths very rarely invade the mucous coat of the gall-bladder, and, as shewn by Siegert's³ and my own figures (*vide* p. 640), are not specially related to the presence of gall-stones. Secondary also contrasts with primary malignant disease of the gall-bladder in the sex incidence: whereas primary carcinoma is about four times commoner in women, secondary growths were much more frequent in the male sex in Siegert's figures. As a rule, secondary growths do not obstruct the cystic duct, but this may, of course, occur and give rise to hydrops of the gall-bladder. Growths of the stomach, duodenum, and colon may spread into the gall-bladder.

¹ Heidenhain. *Verhandl. d. deutsch. Ges. f. Chir.*, 1898, p. 126.

² Beck, C. *Med. Week*, Paris, 1897, v, 137.

³ Siegert. *Virchows Arch.*, 1893, cxxxii, 353.

Flint recorded
29 cases of an
accessory right
hepatic duct

A small accessory hepatic duct opening
into or near the common hepatic duct is said to occur in
12 percent of the cases.
Only 75 per cent of the ^{bodies} ~~cases~~ ^{show}
the usual angular mode of junction
of the Cystic and Common hepatic
ducts (EISENDRATH).

After cholecystectomy the cystic duct
may dilate to form a new
gall bladder and contain calculi
(Eisendrath and Dunsany). Horsmans
finds that destruction or loss of function of
the gall bladder is frequently followed by
dilatation of the Common bile duct

Vide
p. 601

Flint, E. R. Brit. Journ. Surg., Bristol 1928, X, 509
Eisendrath. Boston Med. and Surg. Journ., 1920
CLXXIV, 573

Eisendrath and Dunsany, Surg., Gynec., and
obstet., 1918, XXVI, 110

1 Vide HALL, A. J. Proc. Roy. Soc. Med., 1913, VII,
(Path. sect.), 16.

DISEASES OF THE BILE-DUCTS

ABNORMALITIES.—Atresia or complete obliteration of any part of the bile-ducts is pathological, and usually due to inflammatory changes in fetal life. Abnormalities in the ducts chiefly consist in variation in the length of the cystic and common bile-ducts, and in the presence of abnormal communications between the gall-bladder and the liver (hepato-cystic ducts). The left and right hepatic ducts may remain separate for a considerable distance, and only join when the cystic duct unites with them; in such cases there is no common hepatic duct. The cystic duct may not join the common hepatic duct until close to the duodenum, so that the common bile-duct is very short. A double cystic duct has been recorded (Dreesmann¹). In congenital absence of the gall-bladder (*vide* p. 601) the common bile-duct may be dilated in part of its course.

Variations in the method of opening of the common bile-duct into the duodenum exist; Letulle and Nattan-Larrier² describe four types of the openings of the common bile- and Wirsung's ducts. In some instances the common bile-duct opens into the duodenum ~~separate~~ from the main pancreatic duct. It very occasionally opens with the accessory pancreatic duct of Santorini, the main pancreatic duct being quite separate and opening alone in the position of the normal biliary papilla. In 104 cases Schirmer³ found this four times.

The effect of tight lacing on the biliary apparatus is referred to elsewhere (p. 15).

The Common
bile duct
has also been
found to be
double

away

CONGENITAL OBLITERATION OF THE BILE-DUCTS

Nomenclature.—Most of the cases are associated with cirrhosis, and since, as will be seen later, it is probable that the cirrhosis is the primary change and the cholangitis and obstruction of the ducts secondary and later results, the term "congenital hepatic cirrhosis with obliterative cholangitis" describes these cases more accurately. But since congenital obliteration may possibly be brought about in other ways, it is better to

¹ Dreesmann. *Deutsche Ztschr. f. Chir.*, Leipz., 1908, xcii, 411.

² Letulle et Nattan-Larrier. *Bull. Soc. Anat. Paris*, 1899, lxxiv, 987.

³ Schirmer. *Inaug. Diss.*, Basel, 1893.

retain the more familiar and inclusive title of congenital obliteration of the bile-ducts. Our knowledge of this disease is chiefly due to John Thomson.

Incidence.—In 1892 Thomson¹ referred to 50 cases, and in 1911 Howard and Wolbach² collected 76 cases with necropsies.

Cases resembling this Condition.—Treves³ successfully operated upon a girl aged nineteen for jaundice of sixteen years' duration, and found obliteration and absence of the lower end of the bile-duct. It differs so markedly from all the other cases that it can hardly be included in this group. Jaundice did not begin until the age of three years, instead of either at or shortly after birth. Possibly the obliteration of the duct was due to the effects of a calculus lodging in the duct at or about the time of the onset of jaundice. Thomson⁴ considers that the same morbid process is at work in cholelithiasis in infants as in congenital obliteration of the bile-ducts, and quotes two cases of infantile cholelithiasis in which the biliary apparatus was abnormal (Cuffer, Bouisson).

Etiology.—*Hereditary Influences.*—In a few instances other members of the same family have died soon after birth with jaundice, and it may be suspected with a similar morbid change (Mathie⁵). In Binz's and Gould's cases (quoted by J. Thomson in 1892) two members of a family were proved to have died from this cause. Arkwright's⁶ series of 14 cases of dangerous icterus neonatorum in one family, with 4 survivors, belongs to a different category (*vide* p. 572).

There does not seem to be any real association between *malformations* and this disease. Coneomitant deficiencies in the liver must be regarded as part of the disease, and not as true malformations.

Witzel's⁷ case of a number of true malformations and obliteration of the ducts was possibly congenital cystic disease of the liver (*vide* p. 448). Congenital obliteration of the bile-ducts has been found in association with hypertrophic stenosis of the pylorus (Barker and Mackey⁸). In a case of complete absence of the biliary apparatus in an infant one month old there was a congenital malformation of the left upper arm (Kirmisson and Hébert⁹).

Syphilis is not an important and certainly not more than an occasional cause of the change in the ducts and liver. This is shewn not only by the histological character of the change in the liver, but by the freedom of the parents and patients from signs of syphilis. Among the parents there is evidence of syphilis in very few instances—less than a twentieth (Thomson). While there is every reason to believe that syphilis plays no part in the usual type of the cases, stricture of the ducts may be due

¹ Thomson, J. *Congenital Obliteration of the Bile-ducts*, 1892, Edin.

² Howard and Wolbach. *Arch. Int. Med.*, Chicago, 1911, viii, 559.

³ Treves. *Practitioner*, Lond., 1899, lxii, 18.

⁴ Thomson, J. *Edin. Hosp. Rep.*, 1898, v, 1.

⁵ Mathie. *Glasgow Med. Journ.*, 1906, lxvi, 378.

⁶ Arkwright, J. A. *Edin. Med. Journ.*, 1902, N.S., xii, 156.

⁷ Witzel, O. *Centralbl. f. Gynäk.*, Leipz., 1880, iv, 561.

⁸ Barker and Mackey. *Lancet*, Lond., 1910, ii, 459.

⁹ Kirmisson et Hébert. *Bull. Soc. Anat. Paris*, 1903, lxxviii, 317.

Ward, and Penick 1928, p. 275 - 275
to Penick's 40 cases - 95

In 1916 Holmes collected 108 cases.

and Lawson
Feldman described the condition in ^{of 2 heterologous} one twin

J. F. Ward reported the association with a patent
Septum Ventricleum

Feldman, W. M. and Lawson, M. A. Lancet, 1924, 11, 113

Ward, J. F. Brit. Med. Journ., 1922, 1, 314

Wyand suggests that the choleangitis
is an ascending from the duodenum
due to torrens absorbed from the
lymphatic system

Feldman + Lawson. no *Cholecystitis*, but
not *metastasis*

Wyand. Lancet 1914, ii, 495

to fetal peritonitis, which is usually connected with syphilis; and syphilitic inflammation may attack the walls of the ducts (*vide* p. 658).

Sex.—In Thomson's cases the sex was given in 67, and shewed a preponderance of males—41 males, 26 females.

Pathogeny.—There are two explanations: (i) That there is in the first place a developmental aplasia or a narrowing of the duct, which gives rise by obstruction to cirrhosis; (ii) That there is first a mixed cirrhosis of the liver which gives rise to a descending obliterative cholangitis.

(i) John Thomson¹ believes that in the great majority of cases there is, to start with, a congenital malformation of the ducts which relatively narrows the available lumen; with this view Beneke² and Milne³ agree. This obstruction to the free exit of bile disposes to catarrh, blocking, and finally to obliteration of the ducts. Lavenson⁴ and Parkes Weber⁵ believe that the diverticulum which should form the common bile-duct never becomes pervious. As a result of the obstruction to the passage of bile into the duodenum the bile becomes toxic and biliary cirrhosis is set up.

As a criticism of this view it may be pointed out that cirrhosis of the liver is comparatively rare in association with obstruction of the bile-ducts in adults, and, when present, is usually associated with gall-stones and infection of the ducts which are dilated inside the liver (*vide* p. 331), whereas cirrhosis of quite a different type, and not accompanied by any dilatation of the intrahepatic ducts, is extremely frequent in congenital obliteration of the ducts.

In J. Thomson's 50 cases a microscopical examination was only made in 10 and in all but 1 of these it is stated that cirrhosis was present; in 20 other cases, of which I have notes, cirrhosis was present in 19.

The question therefore arises, is there any evidence that cirrhosis in these cases depends on the obliteration of the larger bile-ducts? If it can be established that the change in the bile-duct is older and more advanced than in the liver, there is fair ground for regarding the hepatic lesion as due to the obstruction in the ducts. Ross⁶ described obliteration of the common bile-duct near the duodenum in a female child, aged three months, whose liver shewed small-celled infiltration around the bile-ducts rather than fibrosis. In this instance the evidence points to the change in the bile-duct being the older. On the other hand, in nearly all the other cases, the fibrosis in the liver is quite as old as the lesion in the bile-ducts.

(ii) The following appears to be a reasonable explanation of the pathogeny of so-called congenital obliteration of the bile-ducts: In the first instance, poisons pass from the maternal placenta to the fetus by the umbilical vein; some of this blood at once passes through the liver, and,

¹ Thomson. *Congenital Obliteration of the Bile-ducts*, p. 38, 1892; and *System of Medicine* (Allbutt and Rolleston), 1908, iv, part i, 106.

² Beneke. *Die Entstellung der kongenital Atresia der grossen Gallengänge*, Marburg, 1907.

³ Milne. *Quart. Journ. Med.*, Oxford, 1911-12, v, 409.

⁴ Lavenson. *Journ. Med. Res.*, Boston, 1908, xviii, 61.

⁵ Weber, P. and Dorner. *Proc. Roy. Soc. Med.*, 1911, iv (Child. Sect.), 41.

⁶ Ross, D. *Lancet*, Lond., 1901, i, 102.

in virtue of the contained toxin, induces multilobular cirrhosis of the liver; the rest of the blood in the umbilical vein passes directly into the general circulation of the fetus by the ductus venosus, and subsequently, by means of the hepatic artery, will convey the same poison to the liver. By this means the toxic body, which may be analogous to toluenediamine, is excreted into the small intrahepatic bile-ducts and sets up cholangitis and unilobular cirrhosis, like that seen in hypertrophic biliary cirrhosis. In this way a mixed cirrhosis (portal and biliary) is induced. The cholangitis descends to the larger ducts, and gives rise to an obliterative cholangitis—a process analogous to obliterative appendicitis. The difference between this condition of congenital (umbilical) cirrhosis with obliterative cholangitis and other forms of cirrhosis in post-natal life consists in the further change in the large bile-ducts and gall-bladder. This additional lesion may be explained as follows: The bile-ducts are extremely small at birth, and any inflammatory change will, from their small size, produce stenosis much more readily than in later life. An analogous effect is seen in the greater incidence of laryngeal obstruction in diphtheria in young subjects than in older patients. The opposed inflamed surfaces of the bile-ducts will also come in contact more readily, and, as in catarrhal appendicitis, obliteration might result.

The following considerations bear on the hypothesis that the disease is primarily a congenital cirrhosis:—

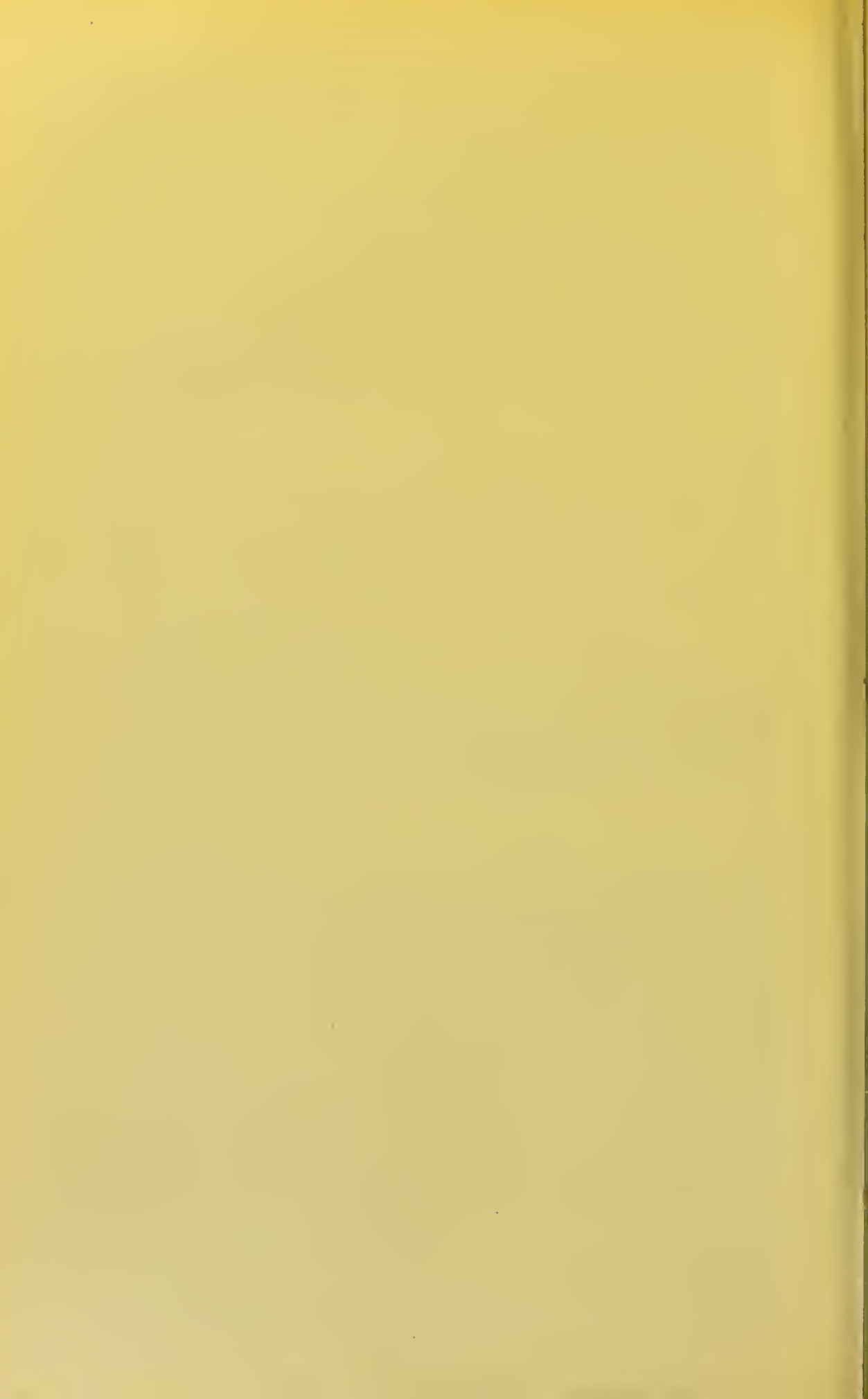
1. The almost constant presence of cirrhosis in these cases of bile-duct obstruction in infants as compared with the infrequency and irregularity with which cirrhosis follows obstruction of the larger bile-ducts in later life.

2. The structural differences between the cirrhosis in congenital obliteration of the ducts, which does not shew any dilatation of the intrahepatic bile-ducts, and the cirrhosis sometimes seen in obstruction of the ducts in later life, in which the intrahepatic ducts are dilated and icteric necrosis of the liver cells is common.

3. The large size of the liver—this resembles hypertrophic biliary cirrhosis. In simple obstruction of the larger bile-ducts in adults the liver, though swollen from retained bile in the early stages, is usually small after death.

4. The large size of the spleen, a phenomenon not met with in uncomplicated biliary obstruction, is best explained as the result of toxic bodies reaching the organ by the splenic artery. In congenital syphilis, in which it is probable that the parasite reaches the liver by the umbilical vein and is derived from the maternal circulation rather than that the ovum is infected by a syphilitic spermatozoon, there is a similar splenic enlargement. The difference between the intercellular cirrhosis of hereditary syphilis and the mixed (unilobular and multilobular) cirrhosis of congenital obliteration of the bile-ducts must depend on a difference in the causes of the two diseases.

5. Against the view that congenital obliteration of the bile-ducts is primarily a form of congenital cirrhosis it might be objected that the poison responsible for the change must pass through the mother, and that she should shew evidence of its influence. In reply it may be suggested that the fetus' liver may be more susceptible than the mother's to poisons tending to produce cirrhosis, just as the effects of syphilis are usually more marked in the child than in its mother.



To sum up, it seems reasonable to believe that the disease is primarily started by poisons derived from the mother and conveyed to the liver of the fetus, and that a mixed cirrhosis and cholangitis are thus set up. The cholangitis accounts for the jaundice, and by descending to the larger extra-hepatic bile-ducts, induces an obliterative cholangitis analogous to obliterating appendicitis. In some cases, especially those fatal early in life, the latter change has not been effected, and cirrhosis alone is found. Possibly in some instances this change never occurs, and in this way some of the cases of cirrhosis in very early life are accounted for. There are probably several conditions at present included under the title congenital obliteration of the ducts, and some, such as D. Ross' case, are due to constriction of the duct by localised peritonitis, and deserve the title better than the cases that are intimately associated with cirrhosis.

Morbid Anatomy.—*The liver* is, in the great majority of the cases, enlarged, and sometimes to a very considerable extent. In my case¹ it weighed twice as much as normal. In only one of Thomson's cases was it definitely stated to have been small. The liver is bile-stained, and often dark green; the surface is usually irregular and has been compared to morocco leather. On section, the organ is tough, firm, and manifestly fibrosed. Cirrhosis was present in nearly all the recorded cases. The lymphatic glands in the portal fissure are usually enlarged.

Microscopically there is well-formed fibrous tissue separating the lobules from each other. The arrangement of the fibrous tissue varies: in parts it is unilobular and separates each individual lobule from its fellows (*vide* Fig. 90); this unilobular fibrosis has been thought to depend on necrosis of the liver cells at the periphery of the lobules (Milne²). In other parts a varying number of lobules are enclosed in firm strands of fibrous tissue. There is thus a mixed cirrhosis composed of the unilobular and multilobular forms. The pseudobiliary canaliculi in the fibrous tissue are prominent, tortuous, and appear to be increased in number. The biliary capillaries between the hepatic cells often contain plugs of inspissated bile. The liver cells are in places well preserved, elsewhere they shew icteric necrosis and do not take the stain.

The Bile-ducts and Gall-bladder.—There is considerable variation both in the situation and the extent of the obliteration of the ducts. Howard and Wolbach describe four groups of cases:—(i) the gall-bladder and cystic duct are patent, but the ducts between the liver and the duodenum are obliterated; (ii) the ducts between the liver and duodenum are patent, but the gall-bladder and cystic duct are absent; (iii) the hepatic and cystic ducts are obliterated; (iv) obliteration at some point in the common duct. They state that by far the commonest situation for obliteration is in the hepatic and cystic ducts; Lavenson found the obliteration most frequent

¹ Rolleston and Hayne. *Brit. Med. Journ.*, 1901, i, 758.

² Milne. *Journ. Path. and Bacteriol.*, Cambridge, 1909, xiii, 135.

^/ pigmentation
and

near the duodenum; and out of 89 collected cases Milne¹ found that the common bile-duct was absent or impervious in 70, the duodenal end being pervious in 5 only; and that in 39 of the 70 the common hepatic duct also was absent or obliterated. The obliterated ducts may be traced in the lesser omentum as fibrous cords which resemble the hepatic artery, and gradually fade off into the surrounding tissues. It is possible that some cases of great cystic dilatation of the ducts (*vide* p. 659) are the outcome of local obliteration of the lower end of the common bile-duct in very early life. The gall-bladder may be collapsed and buried in adhesions, or

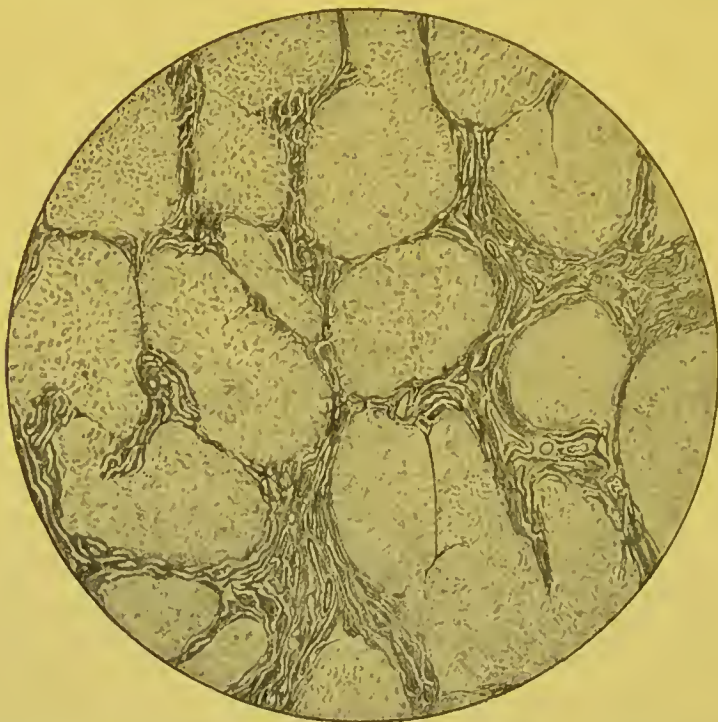


FIG. 90.—Unilobular cirrhosis from a case of congenital obliteration of the bile-ducts in a child aged six months. There is well-formed fibrous tissue, with no sign of recent proliferation, separating the individual lobules. $\times 18$.

thickened and without any cavity. It may contain clear mucus, but rarely bile. In one of Thomson's cases a calculus was found in the gall-bladder.

The Microscopic Appearances of the Ducts.—In my own case the common duct near the point of obliteration shewed great fibrous thickening of its walls, with complete alteration of its normal appearance, its muscular tissue and mucous glands having disappeared. The epithelial lining was lost, and the lumen contained debris and masses of bile-pigment which infiltrated the fibrous walls for a short distance. There was no sign of progressive hyperplasia or inflammation. Thomson (1908) confirms this account. Weber and Dörner described much the same appearances, and in addition embryonic blood-vessels; in the common bile-duct

¹ Milne. *Quart. Journ. Med.*, Oxford, 1911-12, v, 412.

Holmes described obliteration of the cystic duct
by masses of elongated epithelial cells.

Holmes. Johns Hopkins Hosp. Paper, Baltimore. 1909, xviii, 73.



no lumen was found, thus supporting their view that there never had been one.

The *gall-bladder* in Weber and Dorner's case shewed fibrosis and embryonic blood-vessels; in one of Thomson's cases the walls of the gall-bladder, which was partly obliterated, were thickened and infiltrated with young connective-tissue cells; the lining epithelium, where any cavity remained, was described as normal.

The *spleen* is usually enlarged, sometimes very greatly. In a child

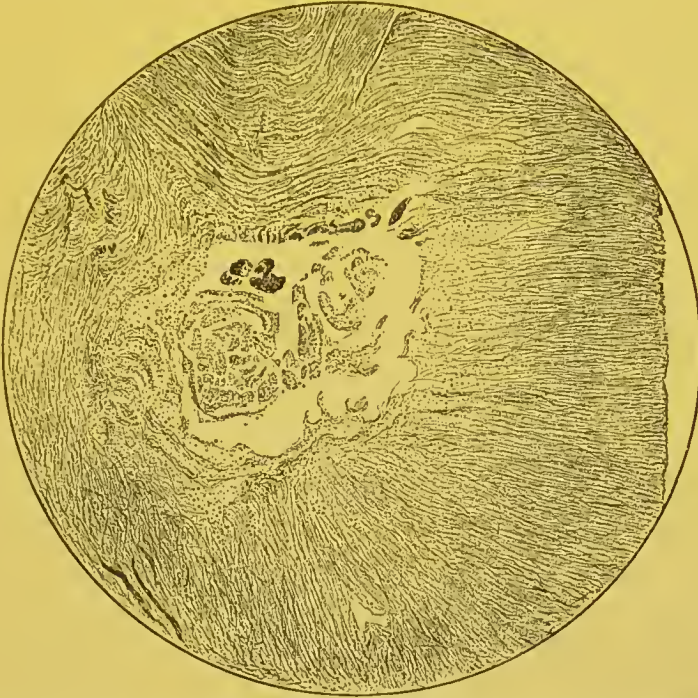


FIG. 91.—Transverse section of common bile-duct close to its obliteration. ($\times 35$.) Shews altered and fibrosed walls of duct, and absence of mucous glands and of the lining epithelium. The small black spots infiltrating the walls of the duct are microscopic masses of inspissated bile, not nuclei.

aged six months recorded by Parker¹ it weighed 5 ounces. It may shew fibrosis (Emanuel²) and excess of plasma cells (Weber and Dorner).

The *Pancreas*.—Periductular fibrosis with intact islands of Langerhans has been described (Cattanco,³ Emanuel, Thomson). The organ has, however, been found to be normal.

The other organs are deeply bile-stained. Adhesions around the liver or bile-ducts are rare, and probably chiefly occur in cases with a syphilitic taint. A small quantity of ascites is recorded in some of the cases, but is very seldom of clinical importance. The cerebrospinal fluid does not contain bile (Weber).

Clinical Picture.—Jaundice may be present at birth or it may succeed

¹ Parker, G. *Lancet*, Lond., 1901, ii, 520.

² Emanuel, *Brit. Med. Journ.*, 1907, ii, 385.

³ Cattanco. *Pediatrics*, Napoli, 1904, 2. s., ii, 584.

what is regarded as physiological jaundice. In some instances the infant does not become jaundiced until two or more weeks after birth. It is conceivable that the effects of congenital changes in the ducts, like those of congenital morbus cordis, may be delayed, and only appear after an interval of some years. If so, cases like Treves' can be explained as belonging to this category. When once established, the jaundice is progressive and eventually may become dark green, but variations may occur, jaundice becoming less for a time and then darker again. There is never much itching.

The urine contains much bile-pigment and stains the napkins. The meconium passed by the infants is usually normal, and is rarely devoid of bile. In only a few instances have the subsequent motions contained stercobilin. As a rule, normal yellow motions are never passed and the stools are clay-coloured from the first. In some instances, however, a green motion has been described after calomel has been given.

This occurrence has given rise to some discussion; it has been suggested that the green colour may be entirely independent of bile, and due to some chemical combination of mercury and sulphur (Thudichum¹), or that the green colour is due to chromogenic micro-organisms (Lesage²). There seems very slender proof that green stools are due to bacterial pigment alone (Garrod, Kanthack, and Drysdale³). It is possible that in the few cases in which the administration of calomel has been followed by a green stool there was biliverdin present and that either there was not complete obstruction of the bile-duct or that the administration of calomel set up ulceration of the intestine and so allowed some bile-stained exudation to pass into the bowel.

Constipation is the rule, but in a few cases diarrhoea has been noticed, and may be due to virulent infection of the alimentary canal.

Haemorrhages from mucous surfaces, into the skin, and from the umbilicus occur in a large number of the cases. Blood may be lost by epistaxis or vomited or passed by the bowel. I have seen fatal haemoptysis. The conjunctivae, which are deeply stained, may shew small haemorrhages. Constant oozing from the umbilicus may occur soon after birth, and is a very grave symptom, since death follows in a few days. In those instances in which more than one child in a family is affected the haemorrhagic tendency is particularly strong (Thomson⁴). Subcutaneous haemorrhages may be scattered all over the body. The haemorrhages, like those seen in other forms of deep obstructive jaundice, in advanced cirrhosis, and in acute atrophy, are due to hepatic insufficiency and the passage of poisons, which should have been stopped by the liver, into the general circulation, to deficiency of fibrinogen and diminished coagulability of the blood, and possibly to degeneration in the vessel walls. Morse and Murphy found the coagulation time of the blood prolonged and a moderate leucocytosis. Weber found the colour-index

¹ Thudichum. *Lancet*, 1889, i, 631.

² Lesage. *Arch. physiol. norm. et path.*, Paris, 1888, 4. s., i, 212.

³ Garrod, Kanthack, and Drysdale. *St. Barth. Hosp. Rep.*, 1897, xxxiii, 13.

⁴ Thomson. *System of Medicine* (Allbutt and Rolleston), 1908, iv, part i, 107.

The blood may show cells containing bile pigment (NEUKIRCH). An indirect van den Bergh's test was reported by Feldman and Lawson

NEUKIRCH. } Zeitschr. f. klin. Med., Berlin, 1912, LXXIV, 380.

This spelling from
original reference

The metabolism of nitrogen
is normal, that of fat is
much disturbed although the
pancreatic juice is normal
(Koplik and CROHN). ^

Koplik and CROHN. Am. Journ. Dis. Child.
Chicago, 1913, V, 36

high (1·2), the red blood-corpuscles increased in size (10μ) and more resistant to haemolysis than normal. In Weber and Dorner's case the Wassermann reaction was negative. The liver is enlarged, and may reach the level of the anterior-superior spine, and is firm, very hard, and fairly smooth. The spleen is usually also enlarged and firm.

The infants usually waste if life is sufficiently prolonged, but careful feeding may delay emaciation, which is not an early symptom. Convulsions may come on before death.

Duration and Prognosis.—A certain number of the cases die within the first few days of life from umbilical or other haemorrhages. Of Thomson's 49 cases, 30 lived more than one month, and of these, 16 survived for upwards of four months, 2 living into the eighth month. Of Lavenson's¹ 62 collected cases only 3 survived eight months, 1 of these lived to eleven months. The end may be hastened by streptococcal infection and resulting haemorrhages. It is clear that the prognosis is extremely bad. Possibly cases with only slight changes survive for long periods, as suggested by Treves and Ashby's² cases (*vide* p. 660). Moreover, other members of a family in which one child has died of the disease may recover from jaundice in early life.

Diagnosis.—Deep jaundice, haemorrhages, enlargement of the liver and spleen, and the absence of any evidence of acute infection in an infant a few weeks old, point to this disease.

Differential Diagnosis.—Since it is usually manifest that the condition is one of severe jaundice, it is hardly necessary to insist on the distinctions from the slight and common jaundice occurring in the first few days of life, in which the faeces contain bile and the jaundice rapidly fades. Persistent deep jaundice is sometimes followed by recovery; in a case of this kind the cause was thought to be very thick bile (Poynton³), a condition which might be due to cholangitis.

From syphilitic disease of the liver, the absence of any history or signs of the disease and the failure of mercurial treatment should distinguish the disease. According to Still,⁴ the liver is much harder on palpation during life in congenital obstruction of the ducts than it is in ordinary cases of syphilis.

From infection of the umbilical vein after birth in which haemorrhage from the navel also occurs, the disease should be distinguished by its much slower course, by the absence of any sign of umbilical infection, and by the fact that at first there may be little constitutional disturbance.

In grave familial jaundice (*vide* p. 572) in which there is no gross obstruction, the faeces are not devoid of pigment, and the liver is not always enlarged.

Treatment is chiefly symptomatic. Small doses of grey powder, fractional doses of calomel, salicylates, or salol may be given to minimise

¹ Lavenson. *Journ. Med. Research*, Boston, 1908, xviii, 61.

² Ashby. *Med. Chron.*, Manchester, 1898-9, x, 28.

³ Poynton. *Rep. Soc. Study Dis. Child.*, 1906, vi, 172.

⁴ Still. *Clin. Journ.*, Lond., 1901, xvii, 324.

intestinal fermentation, and in the later stages salts of calcium to prevent haemorrhage. It is always well to try antisyphilitic treatment on the chance that the disease is of this nature. Very little can be expected from operative measures, and there is considerable risk of haemorrhage, owing to the patient's jaundiced condition. Since the obstruction may be in the hepatic ducts, opening the abdomen to do a cholecystenterostomy is a speculative or "exploratory" operation. Unsuccessful operations have been performed in some cases (Giese, Putnam, Westerman, Morse and Murphy); Ehrhardt¹ united the intestine with the cut surface of the liver, but the infant died six days later. It is true that success followed in Treves' case (*vide* p. 650), but this belongs to a different category.

Since the disease very probably depends on poisons generated in the mother, it is reasonable to treat the pregnant woman with small doses of calomel ($\frac{1}{40}$ to $\frac{1}{20}$ gr.), salol, and other drugs which inhibit intestinal fermentation, and to pay special attention to her diet and general health during pregnancy.

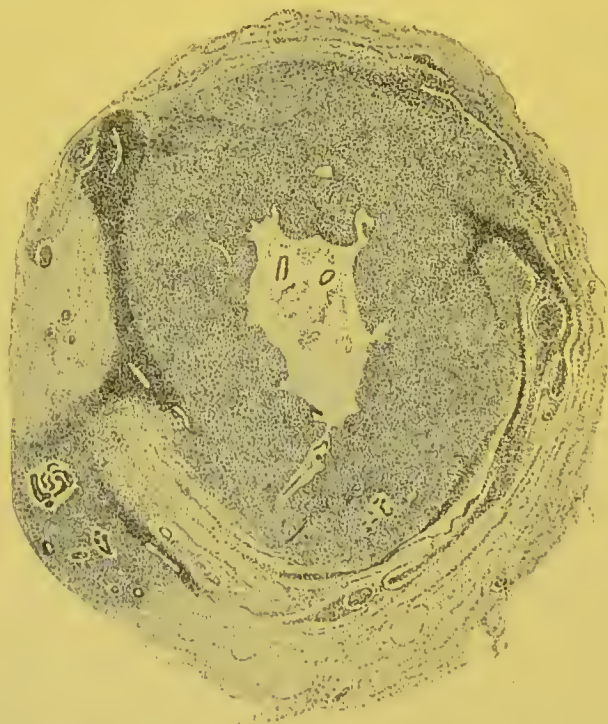


FIG. 92.—Microscopical appearances of congenital syphilitic stricture of the common bile-duct.

Congenital Syphilitic Stricture of the Common Bile-duct.—As the usual form of congenital obliteration of the bile-ducts is not due to syphilis, it is advisable to refer briefly to this rare condition. Beck,² Simonini,³ and others⁴ have described cases. Possibly some of

¹ Ehrhardt, O. *Zentralbl. f. Chir.*, Leipz., 1907, xxxiv, 1226 (Orig.).

² Beck. *Prag. med. Wchnschr.*, 1884, ix, 257.

³ Simonini. *Pediatrics*, Napoli, 1907, 2. s., v, 356.

⁴ *Vide* Milne. *Quart. Journ. Med.*, Oxford, 1911-12, v, 414.

1 / Holmes states from the above 16 per cent of the cases
the hepatic and cystic ducts are normal size in
communication, so that surgical relief would be
possible; but

~~Waller~~ WALLER 35 in 1917 } n
Moxley 41 in 1922,
McWhorter 48 in 1926

McWhorter, G. L. Arch. Surg., Chicago
1924, VIII, 604

WALLER, E. Ann. Surg., 1917, LXVI, 446.
Moxley, J. Brit. Journ. Surg., Bristol, 1920, X, 413
Zipf, K. Arch. f. Klin. Chir., 1923

the reported cases of stricture of the common bile-duct in early life, especially those that improved under mercury, may have been of this nature.

My case¹ was a female child three weeks old, deeply jaundiced, emaciated, bleeding from the bowel, and resembled congenital obliteration of the ducts. The liver was much enlarged and hard, and the spleen was palpable. At the necropsy the lower half-inch of the common bile-duct was thickened and formed a white cord about the size of an adult's vas deferens; on transverse section it resembled the cross-section of the stem of a clay pipe, there being a small round hole in the centre. The microscopic appearances are seen in Fig. 92. The liver shewed intercellular cirrhosis. The pancreas was enlarged, firm, and white, and shewed extreme interacinous fibrosis, the islands of Langerhans being prominent and well preserved.

DILATATION

OBSTRUCTION in the course of the common bile-duct leads to dilatation of the common and other bile-ducts. Whatever the nature of the obstruction, dilatation will occur, but, generally speaking, it is less when due to a gall-stone in the common duct than when pressure is exerted from without by a tumour, such as carcinoma of the pancreas. The explanation of this is that in cholelithiasis the obstruction is not so complete as in the case of tumours. Mayo Robson² and Swain³ have recorded cases of excessive dilatation of the common duct due to gall-stones. The extent of the dilatation of the biliary duct varies considerably, but it is usually greatest in the common bile-duct above the obstruction; it may be universal, and implicate the intrahepatic bile-ducts widely. Exceptionally a large cyst of the common bile-duct results. The contents of the dilated ducts may be bile or clear mucus; in gall-stone obstruction of the common duct it is very rare to find clear mucus in the ducts. Lenormant⁴ could find only two such cases recorded. Colourless mucus in the ducts is usually associated with the pressure of a neoplasm on the common bile-duct.

CYSTIC TUMOURS

In rare instances, of which Mathieu⁵ collected 20 examples in 1908, and Lavenson⁶ 29 in 1909, great dilatation of the common bile-duct, forming a gigantic cyst, occurs; it is usually seen in children. There may not be any obvious obstruction, and the condition has been spoken

or of the other extrahepatic ducts. The common hepatic duct was affected in cases reported by Zipp and Eliacher

¹ Rolleston. *Brit. Med. Journ.*, 1907, ii, 947.

² Mayo Robson. *Diseases of the Gall-bladder*, p. 196, ed. iii, 1904.

³ Swain, W. P. *Lancet*, Lond., 1895, i, 743.

⁴ Lenormant. *Rev. de gynéc.*, Paris, 1912, xviii, 175.

⁵ Mathieu, P. *Rev. de chir.*, Paris, 1908, xxxvii, 61.

⁶ Lavenson. *Am. Journ. Med. Sc.*, Phila., 1909, cxxxvi, 563.

ought to be
to obstruction

it/λ

of as "idiopathie" and compared to congenital hydronephrosis (Russell¹). In some cases, there has been a valve-like fold of mucous membrane at the lower end of the common bile-duct; (this) has been thought to be the cause of the obstruction (Roslowzew²); but it may merely be secondary to kinking produced by the cyst. If, as in congenital morbus cordis, changes initiated during fetal life can remain latent for years and then, possibly as the result of slow cicatricial contraction of inflammatory tissue, give rise to obstruction, a satisfactory explanation is obtained of cases (Ashby,³ Oxley,⁴ Lavenson) in which the lower end of the common bile-duct was obliterated.

A girl aged seven had been jaundiced for two and a half years, and more recently had been tapped to the extent of 50 ounces for ascites. She was emaciated and had oedema of the feet. A cyst on the right side of the abdomen was tapped and 16 pints of dark-green mucus came away. In the course of three months it was tapped ten times, and on each occasion 8 to 10 pints were removed. After death the cyst was found to be the dilated common bile and cystic ducts; the common bile-duct was obliterated near the duodenum (Ashby).

Possibly in the following case obstruction in the common duct was due to ~~hereditary~~ syphilis:—

Congenital/λ

In a deeply jaundiced child aged nine years there was very marked evidence of hereditary syphilis in the body generally, and in the liver in intercellular cirrhosis. The liver and biliary apparatus preserved in the Museum of the College of Medicine, Newcastle-on-Tyne (No. 382-2), shew the common bile-duct dilated to the size of one's fist, the cystic and hepatic ducts being also dilated; the gall-bladder is atrophied and collapsed, and the opening of the common bile-duct into the duodenum cannot be found.

Some of the recorded cysts have been extraordinarily large, and when first seen on opening the abdomen, have resembled ovarian or hydatid cysts. The fluid inside them contains bile-pigment.

In Vater's⁵ case of an infant, aged one year, enormous dilatation of the common duct was due to obstruction produced by an indurated pancreas. Todd⁶ described a similar case in a girl aged fourteen years. In Wilks and Moxon's⁷ case (*vide* p. 687), the common bile-duct of a child aged four years, which was so dilated as to be as big as its head, contained pendulous growths. In a woman aged forty-six years a cystic dilatation, containing 148 ounces of bile, was regarded by Eve as due to valvular obstruction produced by a papilloma growing from the wall of the common bile-duct one inch above the biliary papilla. Papillomatous growths may, however, be secondary to irritation inside a cyst.

¹ Russell. *Ann. Surg.*, 1897, xxvi, 692.

² Roslowzew. *Deutsche med. Wchnschr.*, 1902, xxviii, 739.

³ Ashby. *Med. Chron.*, Manchester, 1898-9, x, 28.

⁴ Oxley. *Lancet*, Lond., 1883, ii, 988.

⁵ Vater, Abraham. *Diss. de scirrhis viscerum*, Vitemb., 1723. Quoted by Frerichs, *Diseases of Liver*, ii, 468, Transl. New Syd. Soc., 1861.

⁶ Todd. *Dublin Hosp. Rep.*, 1817, i.

⁷ Wilks and Moxon. *Pathological Anatomy*, p. 485, 3rd ed., 1889.

~~It~~ ascribed to primary weakness of the wall of the duct (Levermore), It has been compared to congenital hydronephrosis (Russell) and to idiopathic dilatation of the oesophagus (Bohmansson), so possibly it may be the result of failure, from nervous inco-ordination, of Oddi's ~~sphincter~~ sphincter at the lower end of the common bile duct to relax (achalasia).

^/biliary.

2/ In Eliöcher's case there was an anatomical anomaly of the bile ducts. Some congenital factor has been widely assumed, such as weakness of the walls of the common duct, or the presence of abortive diverticula, like that of the growing ruse to the pancreas, from the common duct, and in support of this such diverticula and even spindle celled dilatation of the common duct have been found in foetuses. Budde regards these diverticula as accessory gall-bladders.

Morbid Anatomy. The cyst may be spheroidal or pear-shaped, but is usually spindle shaped, the lower end of the common bile duct ~~not~~ being dilated, though it may turn an abnormal course which, however, may be secondary to and not the cause of the cyst.

In 30 out of Mr. Lohr's 48 cases the hepatic

ducts showed dilatation.

In Söderlund's case there were two idiopathic cysts of the common bile duct, one spindle-shaped, the other a diverticulum; the ducts and the gall-bladder contained numerous small calculi.

Bohmansson, G. Acta chirurg. Scandinav., 1924, LVI, 440.

Budde, D. Arch. f. klin. Chir., 1924, CXX,

Söderlund, G. Acta chirurg. Scandinav., Stockholm, 1925, LIX, 253.

They are latent for long periods.

It may be constant or more often, intermittent; McWhorter found it constant in 13, intermittent in 23.

and Morley, McWhorter
Waller/unsust~~ed~~ that the
Cyst should be drained
into the intestine and
avoided death to
external drainage.

(71 per cent.
Operation
most safe)

KEHR, | 1

KEHR. Diagnosis of Gall-stone Disease,
American Transl. p.48, 1901 |

Out of ⁴¹~~29~~ cases of this condition ³⁶~~18~~ were in females and ~~2~~ only in males. In 22 cases in which the age was given the average age was fifteen years and eight months (Lavenson).

Clinically these cases present themselves as abdominal cysts in connexion with the liver and may be regarded as a dilated gall-bladder, or as pancreatic, hydatid, or ovarian cysts. ^{of an} Jaundice is present, but in a female child aged sixteen months under my observation there was no jaundice. Pressure on the portal vein or inferior cava may explain ascites and oedema of the feet. The prognosis and treatment are unsatisfactory; out of 22 cases, ~~operated upon, 12 died.~~ Drainage of the cyst and exploration of the lower end of the common bile-duct with a probe so as to displace any valvular-fold of mucous-membrane and allow a free passage of bile into the duodenum have been employed. ^{and} Eve¹ considered anastomosis of the cyst with the hepatic flexure of the colon the simplest and safest course.

cyst and drained externally, a proved fatal (Mony)

(Mony)
The three cardinal signs are jaundice, a tumour on the right hypochondrium, and belly pain.

Intra-duodenal Bile-containing Cyst in Communication with the Ampulla of Vater.—R. S. Trevor² described a cyst containing bile, the size of a tangerine orange, which projected into the duodenum in the situation of the biliary papilla. It was lined inside and out by mucous membrane and its only communications were with the ampulla of Vater and with the duodenum. It appeared to be due to a congenital fusion in the middle line of two folds of duodenal mucous membrane which are often normally present on either side of the biliary papilla. Normally these folds enclose a fossa, but fusion of the folds would convert the fossa into a cyst; as the fusion was not everywhere complete, a bile-containing cyst communicating both with the biliary papilla and the duodenum resulted. It was found in the body of a man, aged twenty-four years, who died in St. George's Hospital from a perforated duodenal ulcer. There was no jaundice and no gall-stone.

SIMPLE STRICTURE

WITH the exception of the cystic duct, this is very rare. The cases may be divided into two groups: (i) the congenital cases, described on page 649, and (ii) those acquired in later life, which will be dealt with here. It is possible that in some of these cases a slight congenital change in the ducts might gradually progress so that it would only give rise to bad effects some years after birth (*vide* p. 660).

Incidence.—It is generally assumed that ulceration of the common duct due to gall-stones may, by cicatricial contraction, lead to stenosis, but this sequence is surprisingly rare. The stricture is usually localised, but it may be diffuse (Courvoisier, Mathieu³), or there may be more than one stricture. ^{and} Körte⁴ and Moynihan⁵ have recorded cases, and a good

¹ Eve. *Trans. Clin. Soc., Lond.*, 1906, xxxix, 144.

² Trevor. *Trans. Path. Soc., Lond.*, 1905, lvi, 138.

³ Mathieu. *Rev. de chir.*, Paris, 1908, xxxvii, 175.

→ ⁴ Körte. *Beitr. z. Chir. Gallenweg.*, S. 341, 1905, Berlin.

⁵ Moynihan. *Brit. Med. Journ.*, 1905, ii, 1390.

example of a tight stricture of the common duct with a soft calculus just above it, in a woman aged twenty-six, is described in St. Thomas's Hospital Reports.¹ In the cases of simple stricture recorded by Holmes² and Moxon³ the stricture was at the commencement of the common hepatic duct and therefore not much exposed to calculi, except small bilirubin-calcium calculi. In Moxon's, Johnson's,⁴ and Phillips's⁵ cases there was no history of cholelithiasis. In the following case the termination of the common bile-duct was obliterated, apparently from cicatrization of an ulcer due to gall-stones:—

A woman aged forty-six years was operated upon for recurrent attacks of biliary colic. The gall-bladder was empty and contracted, but the cystic duct was dilated by five calculi, which were removed. The cystic duct was united to the abdominal wound, and bile was discharged for ten days. The patient then got worse and died suddenly. At the necropsy the common bile-duct was dilated and contained several calculi; its opening into the duodenum was completely obliterated by cicatrization of an ulcer.⁶

Stricture and obliteration of the cystic duct in cholelithiasis and cholecystitis are comparatively common, and thus form a marked contrast to the other large bile-ducts.

It is conceivable that in some cases simple stricture is due to ulceration following cholangitis set up by typhoid or influenzal infection. Possibly syphilitic inflammation may account for some of the cases. Lazarus-Barlow⁷ recorded a case of stricture in a boy the subject of hereditary syphilis, but in this instance and in that described by H. Mackenzie⁸ the cicatricial process probably started outside the ducts and compressed them from without (*vide* p. 380). Mathieu refers to ~~two~~ cases of post-operative stricture of ~~the common bile duct after cholec-~~
~~dochotomy~~. The following is the only case of simple stricture of the common bile-duct which has been detected at St. George's Hospital in the last twenty-four years:—

Eliot

A man aged sixty years, with chronic jaundice, was admitted with pneumonia which proved fatal. There were a fibrous stricture of the common bile-duct in its lower fourth and great distension of the gall-bladder and bile-ducts. There was no evidence of any malignant disease or of gall-stones.

Some cases of stricture of the bile-ducts in adults may, in the absence of microscopical examination, have been cases of primary carcinoma of the ducts, as a stricture which, to the naked eye, appears merely fibrous, may be carcinomatous.

¹ *St. Thomas's Hosp. Rep.*, 1901, xxix, 169.

² Holmes, T. *Trans. Path. Soc.*, Lond., 1858, ix, 130.

³ Moxon, W. *Ibid.*, 1873, xxiv, 129.

⁴ Johnson, G. *Brit. Med. Journ.*, 1880, ii, 200.

⁵ Phillips, S. *Trans. Clin. Soc.*, Lond., 1888, xxi, 26.

⁶ *St. Barth. Hosp. Rep.*, 1899, xxxv. Surg. Registrar's Report, p. 216.

⁷ Lazarus-Barlow, W. S. *Trans. Path. Soc.*, Lond., 1899, l, 158.

⁸ Mackenzie, H. *Ibid.*, 1892, xliii, 84.

Elliot refers to 35 cases of benign stricture
due to the inflammatory effects of gall stones

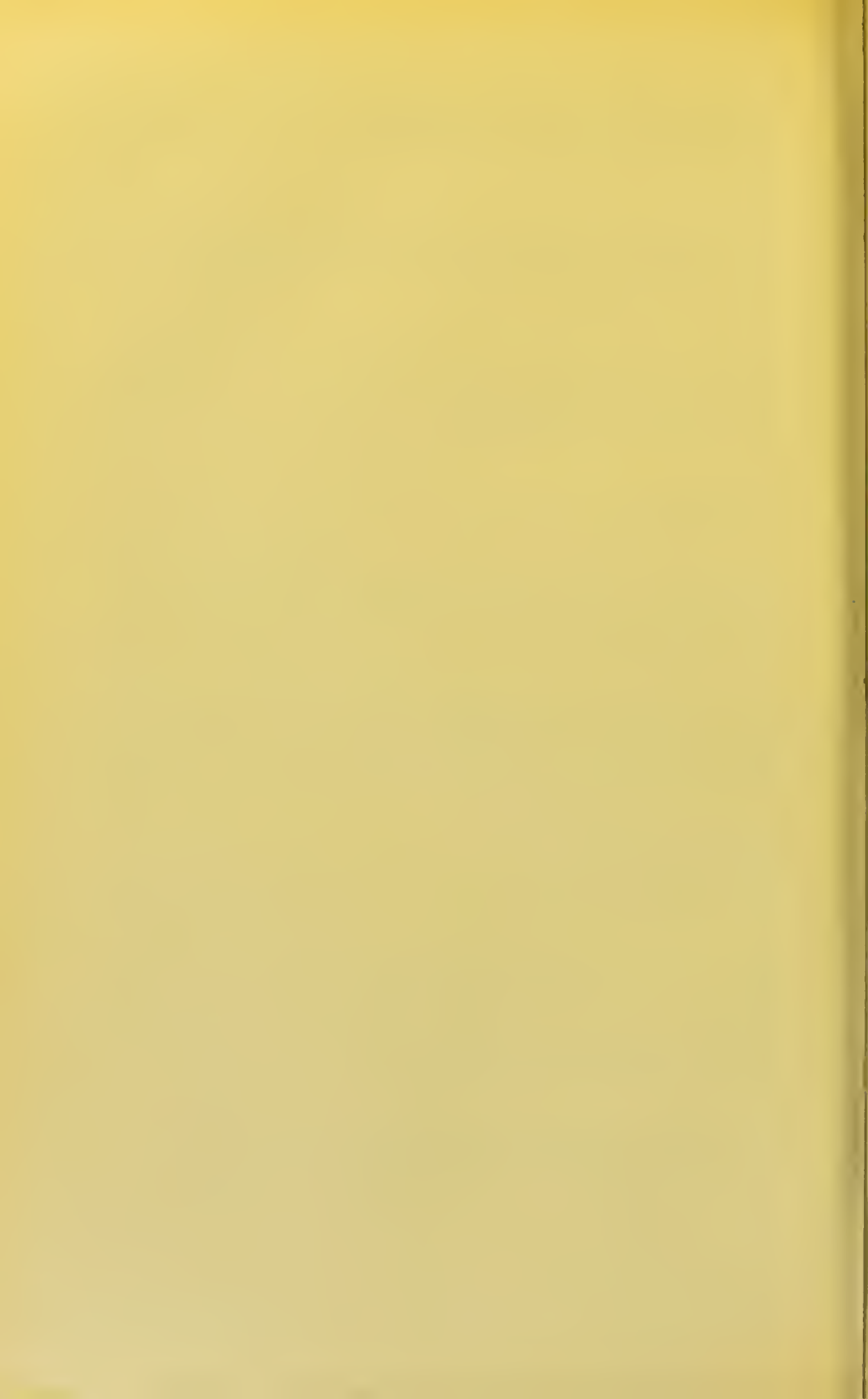
Out of Elliot's 45 cases of simple stricture - 31 were at the junction of the cystic
and common hepatic duct, 9 in the common duct, and 5 in the common hepatic duct.

^; this may have been the cause in Hall's case
of obliteration of the hepatic duct.

segmental excision of the ducts and stasis
that it is very prone

Elliot, E. Surg., Gynec., and Obstet., 1918, XXVI, 81

Hall, A.-J. Proc. Roy. Soc. Med., 1913, VII, (Path. Sect.), 16.



In a woman aged fifty-seven the lower part of the common bile-duct was much stenosed as if from cicatrisation of an ulcer due to gall-stones, but microscopically it was carcinomatous.¹ Andral² described as inflammatory cases which were probably carcinomatous.

The symptoms are those of chronic obstructive jaundice and resemble those of malignant disease of the bile-ducts. In Moxon's case, in which jaundice lasted eight months, there was xanthoma multiplex on the hands, back, and scrotum. ~~An accurate diagnosis is impossible before the abdomen is opened and the duct freely exposed.~~

mecongestional medication
other cases
Treatment.—If there is any suspicion of syphilis, ~~iodides~~ should be given. ~~Failing any improvement from antisyphilitic treatment, an exploratory operation with a view of resecting the stricture, or uniting the gall-bladder with the intestine, if the stricture is in the common bile-duct, should be undertaken.~~

SYPHILIS.—Stricture of the ducts due to congenital syphilis, the pressure of a gumma, syphilitic adhesions (p. 365), syphilitic adenitis (p. 552) and pancreatitis (p. 560), are referred to elsewhere.

CATARRHAL JAUNDICE OR ACUTE CATARRHAL CHOLANGITIS

CATARRHAL JAUNDICE is usually regarded as due to a local inflammatory swelling of the mucous membrane of the biliary papilla and the termination of the common bile-duct, which leads to biliary obstruction and to the passage of bile into the circulation.

It is essentially due to a local inflammatory obstruction, and must be distinguished from toxæmia and infectious jaundice (Weil's disease) which are the manifestations of a general toxæmia or hæmic infection. While giving this view as to the nature of acute catarrhal jaundice, there is room for discussion as to the part played by infection and inflammation spreading from the duodenum. Gastro-duodenal catarrh may be toxic or due to microbic activity, and in the latter case the jaundice might be spoken of as infective. The French school,³ indeed, includes catarrhal jaundice among the benign forms of infective jaundice. Besides mechanically obstructing the lower end of the bile-duct, the morbid process may extend upwards and involve a greater or lesser extent of the common bile-duct. When a considerable extent of the common bile-duct is inflamed, the condition usually becomes one of chronic cholangitis and clinically presents itself as one of prolonged catarrhal jaundice. The explanation of catarrhal jaundice given above has been often questioned,

¹ Krokiewicz. *Wien. klin. Wchn.*, 1898, xi, 321.

² Andral. *Clinique médicale*, Paris, 1831, iv, 500.

³ Chauffard. *Traité de médecine* (Bouchard, Brissaud), 1902, v, 89.

and it has been thought that the real cause is catarrhal pancreatitis, which compresses the common duct (Oser,¹ Mayo Robson²). It is probable that so-called catarrhal jaundice may be of two kinds: (i) due to inflammation of the biliary papilla and lower end of the common bile-duct, or cholangitic jaundice; (ii) due to swelling of the head of the pancreas, pancreatic jaundice.

Causation.—Gastro-duodenal catarrh involving the mucous membrane of the biliary papilla readily spreads into the common channel, or ampulla of Vater, inside the biliary papilla. Comparatively little swelling of the mucous membrane of the narrow orifice of the papilla is sufficient to obstruct the flow of bile through it, and a plug of tenacious mucus may easily form in the lumen of the papilla. Probably this is what happens in the ordinary run of cases, though it is not improbable that inflammatory swelling spreads a varying distance up the common bile-duct or into Wirsung's duct, producing swelling of the head of the pancreas, in more prolonged examples of the disease. Some cases, which apparently begin as catarrhal jaundice, rapidly pass into acute yellow atrophy, and it is possible that inflammation of the lower end of the common duct has extended up to the liver.

The causes of catarrhal jaundice are, therefore, those of gastro-duodenal catarrh; it is a complication of acute gastritis and may be due to alcoholic excess or indiscretions in diet, and follows chills.

Since gastritis is very common in the specific fevers, it is easy to understand that jaundice in the course of enteric fever or pneumonia may depend on purely local obstruction at or near the biliary papilla. On the other hand, jaundice in the course of the specific fevers may be toxæmic, or depend on infection of the bile-ducts and gall-bladder. In enteric fever jaundice is remarkably rare—so much so that Sir W. Jenner³ never met with it. When it does occur, it may be catarrhal, toxic, or due to infective cholangitis. Catarrhal jaundice may be met with at any period in the course of typhoid fever or in a relapse, and in no way affects the course of the disease.

Da Costa,⁴ in a review of 52 cases of jaundice in the course of enteric fever, found 4 due to catarrhal jaundice. Among 1500 cases of enteric fever at the Johns Hopkins Hospital there were 8 cases of jaundice, apart from cholecystitis (T. M'Crae⁵). In 244 cases of enteric, which I analysed, at the Imperial Yeomanry Hospital, Pretoria, there was one case of mild catarrhal jaundice.⁶ I have seen similar cases in England.

Catarrhal jaundice may supervene in the course of portal cirrhosis and be due to gastro-duodenal catarrh, which is favoured by chronic

¹ Oser. Nothnagel's *Handbuch*, 1898, xviii, Th. 2, 111.

² Robson, Mayo. *Lancet*, Lond., 1904, i, 773; and *Montreal Med. Journ.*, 1904, xxxiii, 741.

³ Jenner, W. *On Fevers and Diphtheria*, p. 353, 1893.

⁴ Da Costa. *Am. Journ. Med. Sc.*, 1898, exvi, 1.

⁵ M'Crae. *System of Medicine* (Osler and M'Crae), 1907, ii, 136.

⁶ Rolleston. *Brit. Med. Journ.*, 1901, ii, 976.



7
and it has been suggested that the
simple catarrhal jaundice ~~commonly~~
attributed to gastro-duodenal
catarrh, is in most instances the
sporadic form of epidemic
catarrhal jaundice (Cockayne
and a benign infection (Jones
and Minot)

Cockayne. Quart. Journ. Med., Oxford, 1912-13

Jones, C.M. and Minot, G.R. Boston Med. and Surg. Journ., 1923, ^{VI, 1}
CLXXXIX, 531.

portal engorgement and may be lighted up by alcoholic excess. A slight icteric tinge of the skin is very frequent in advanced mitral disease; it is only exceptionally that there is intense jaundice. It may also occur and be perhaps the first symptom in malignant disease involving the liver or bile-ducts.

Thus in two cases under my care in St. George's Hospital at the same time in 1897 jaundice came on suddenly with vomiting and gastro-enteritis: one was a woman with primary carcinoma of the gall-bladder; the other, a man with primary carcinoma of the common bile-duct. In both cases the jaundice lasted until death.

Catarrhal jaundice may also complicate other organic diseases of the liver, such as hydatid. Emotional jaundice has been thought to be catarrhal in origin, but without sufficient grounds. Catarrhal jaundice may be epidemic ~~because gastro-duodenal catarrh is epidemic. Epidemic jaundice, however, is usually due to infection of the ducts. As examples of epidemic infective jaundice, Weil's disease (vide p. 597) and jaundice following drain poisoning may be mentioned.~~ It is not always easy to be dogmatic as to the nature of mild epidemic jaundice; probably most cases are infective rather than due to local catarrh of the lower end of the common bile-duct. ~~Probably~~ different micro-organisms may give rise to ordinary catarrhal jaundice; from investigation of the serum reactions in a number of cases Sacquépée and Fras¹ found specific agglutination for *Bacillus typhosus*, *B. paratyphosus* type A, and the colon bacillus. In some instances no specific agglutination was obtained. Jaundice resembling the catarrhal form may be due to infection of the ducts with *B. typhosus* without any symptoms of enteric fever (Étienne and Thiry²). d1

Morbid Anatomy.—Opportunities for investigating the morbid conditions are rare, and only arise when death occurs from some other cause, such as an accident. The mucous membrane of the duodenum, the ampulla of Vater, and adjacent part of the common bile-duct is swollen, injected, and covered by tenacious mucus; a plug of inspissated mucus may be found in the orifice of the biliary papilla. These changes rarely extend further up than the lower end of the common bile-duct. The swelling of the mucous membrane may, however, subside after death, and because it is possible to force bile into the duodenum by pressure on the gall-bladder it does not follow that there was no obstruction during life. The same remark applies, but with more force, to the passage of a probe up the bile-duct from the duodenum. Eppinger³ found hyperplasia of the lymphoid tissue of the mucosa of the lower end of the bile-duct in a patient who died from an accident on the eighth day of jaundice. He compared the condition to tonsillitis. Catarrhal inflammation and swelling of the head of the pancreas have been found during operations on cases of prolonged catarrhal jaundice (Robson). The liver may be swollen

¹ Sacquépée et Fras. *Compt. rend. Soc. Biol.*, Paris, 1905, lvii, 533. /f.c.

² Étienne et Thiry. *Arch. gén. de méd.*, Paris, 1907, excviii, 97.

³ Eppinger. *Wien. klin. Wchnschr.*, 1908, xxi, 480.

from accumulation of bile and from vascular engorgement. The lining membrane of the heart and vessels is bile-stained.

Clinical Picture.—*Incidence.*—In an analysis of 215 cases of simple catarrhal jaundice Neumann¹ found that 42 per cent occurred in the first ten years of life, but sucklings are rarely attacked. Ten per cent of the cases occurred in the second, and 27 per cent in the third decade. It is commoner in the winter than in the summer.

Premonitory Symptoms.—Before jaundice appears there are usually, though not invariably, signs of gastro-intestinal disturbance which may last for a few days to a week. These are vomiting, loss of appetite, furred tongue, foul breath, bitter taste in the mouth, headache, vertigo, dyspepsia, some general malaise, and occasionally flying pains in the limbs. Diarrhoea from extension of the catarrh to the intestines is often seen. The motions become clay-coloured before the appearance of icterus and markedly offensive. Contrary to what might be anticipated, Cammidge² found that stercobilin is constantly present. The faeces may remain pale for a considerable time; this may depend on milk taken as food, and on the faeces containing gas in a finely divided state. Jaundice may not be noticed by the patient until his attention is directed to it by his friends. The conjunctiva is the first part of the body to shew the icteric tint, but the presence of bile-pigment can be detected in the urine even before this. The fatty and often slightly yellow masses (pingueculae) underneath the conjunctivae at the canthi must not be mistaken for icteric tingeing. The face becomes jaundiced soon after the conjunctivae. This is more manifest in blonds than in dark-skinned persons who are often naturally somewhat sallow. The oral mucous membrane, especially under the tongue and on the inner surface of the lips, appears yellow when the blood is pressed out of the superficial vessels. From the face the yellow tint spreads to the trunk and extremities, reaching the legs last; the whole of the body finally becomes jaundiced, and sometimes of a bright yellow colour. The dark green colour seen in obstructive jaundice due to malignant disease is never seen in catarrhal icterus; but the skin may shew the effects of jaundice for a considerable time.

Osler³ mentions a case in which stigmata or spider angiomas appeared on the face during catarrhal jaundice.

By the time that jaundice has appeared, the gastric symptoms have usually begun to subside. This, however, is by no means universal. Obstinate vomiting may persist if the diet is not carefully restricted and supervised. At the onset there may be fever, ~~from the gastro-enteritis,~~ but otherwise the temperature is either normal or below the normal. ~~It is probable that cases which otherwise resemble catarrhal jaundice but shew a raised temperature for more than two or three days are mild cases of toxæmic or infective jaundice.~~

¹ Neumann. *Deutsche med. Wchnschr.*, 1899, xxv, 574.

² Cammidge. *Proc. Roy. Soc. Med.*, Lond., 1910, iii (Med. Sect.), 185.

³ Osler. *Johns Hopkins Hosp. Bull.*, Balt., 1901, xii, 337.

/ or respiratory disturbance

From duodenal lavage Jones and Minot find that in the early stage there is obstructive jaundice with little or no bile in the duodenum, but that this is followed by a, as clinical improvement occurs, by an abnormally high output of bile into the intestine, 3 to 5 times the normal, with the presence of an abnormal pigment cholecyanin. Their excretion and disordered secretion is due to disturbance of bile pigment metabolism in the liver.

usually not above 100°F

Van den Bergh's test shows that there is probably a combination of toxic-infective with obstructive jaundice (M^{rs} Nee). There is often a fall in the red blood count and haemoglobin. Jones and Minot describe slight leucocytosis in the early stage, followed by leucopenia with at the height of the jaundice a relative increase in the lymphocytes (50 per cent.) and the large mononuclears, immature and vacuolated leucocytes being common.

Symptoms when the Disease is Fully Developed.—The pulse is slow ; it is often 60 or less per minute, and is of low tension, soft, and may be dirotic. The slowing of the heart's action is much less marked in children than in adults. Pruritus is often troublesome, and the scratching may lead to traumatic eczema, or even to an urticarial rash. It is rare in children. Its mechanism is discussed on p. 546. Yellow vision (xanthopsia) is rare ; its existence is seldom a cause of complaint, but the patients may be found to have noticed it on being questioned (*vide* p. 546). ~~The action of the bile constituents on the brain causes mental depression and, sometimes, a melancholic condition, There may be much irritability and incapacity for transacting the ordinary affairs of life efficiently~~ *may be present*

The urine contains bile-pigment. On shaking it in a white porringer the foam becomes characteristically yellow. During the first few days and even before jaundice has appeared bile acids as well as bile-pigment may be present in the urine. In 12 cases indican was present in all (Simon¹). During the period of the disease when the patient feels worst there may be a distinct excess of nitrogen in the urine as compared with that taken in. During this time the patient loses weight. While there is bile in the urine casts may be found, but not albumin. Out of Cammidge's 53 cases of catarrhal jaundice 13 shewed excess of urobilin and 26 calcium oxalate crystals. Cammidge² obtained a positive pancreatic reaction in 42 out of 53 cases ; and Garrod³ recorded an instance of glycosuria during catarrhal jaundice. These observations support the view that in some cases the jaundice may be due to pancreatitis.

The occurrence of bile-pigment in the saliva in cases of jaundice has been recorded by various authors, especially when, as a result of mercurial treatment, inflammatory changes in the mouth are superadded. W. Legg⁴ always found the saliva colourless in uncomplicated jaundice. The sweat, especially from the armpits, may contain bile-pigment, but generally the perspiration is colourless. The secretion of the alimentary canal, the tears, nasal mucus, and in women the milk, are, in spite of statements to the contrary, free from bile. In inflammatory conditions the altered secretions and exudations become bile-stained ; this is shewn in pneumonic sputum and in pleural and peritoneal effusions.

The blood-serum contains bile-pigment, ~~but there is no change in the corpuscles. In 27 cases the red count was normal or even above normal in 16, and the leucocyte count was 10,000 or below in 20 (Emerson⁵). Occasionally there is slight leucocytosis at the onset. As has been pointed out above (p. 544),~~ The serum of jaundiced patients has been said to agglutinate typhoid bacilli. Agglutination of paratyphoid bacilli ^{1) and} has also been observed (Saequépée and Fras⁶).

¹ Simon. *Amer. Journ. Med. Sc.*, Phila., 1895, cx, 173.

² Cammidge. *Proc. Roy. Soc. Med.*, Lond., 1910, iii (Med. Sect.), 171.

³ Garrod, A. E. *Lancet*, Lond., 1912, i, 560.

⁴ Legg, W. *St. Barth. Hosp. Rep.*, 1877, xiii, 12.

⁵ Emerson. *Clinical Diagnosis*, p. 586, 1906.

⁶ Saequépée et Fras. *Compt. rend. Soc. Biol.*, Paris, 1905, lvii, 533.

As a rule, there is no hepatic enlargement or tenderness. Many authors state that the liver may be enlarged in simple catarrhal jaundice as the result of distension of the intrahepatic ducts with bile, but if the enlargement is at all marked, it is probable that inflammation of the common bile-duct has spread to the ducts in the liver substance. The gall-bladder is sometimes palpably enlarged, but considerable enlargement should suggest that the disease is cholecystitis with some inflammation of the common bile-duct.

Duration.—The jaundice gradually fades in the course of four to six weeks, but the skin may be tinged for a considerable period. In slight attacks the icteric tint may pass away in a couple of weeks. Occasionally cases, which begin like ordinary catarrhal jaundice and eventually clear up, hang fire and last for months; Chauffard¹ quotes cases lasting from ninety-two to one hundred and fifty-five days. These cases are either examples of chronic catarrhal cholangitis, and allied to the chronic inflammation of the common bile-duct set up by calculi (*vide* p. 759), ~~as~~ is shewn by the occurrence of intermissions, ~~or~~ due to pancreatitis (Robson²). ^{~ (11)} Thus, though beginning like catarrhal jaundice, these cases must be regarded as complicated by an extension of the inflammatory process and as belonging to another category. If, in a case regarded as catarrhal jaundice, the disease does not clear up, there is either some complication or the diagnosis is wrong. Relapses of catarrhal jaundice may occur.

Effects.—Considerable loss of weight occurs in well-marked catarrhal jaundice. Loss of appetite and the resulting deficiency in the intake of food partly accounts for this, but the diminished absorption of fats is also an important factor.

Calculi and biliary colic may follow ordinary catarrhal jaundice, but in order to explain cholelithiasis as a sequel of ordinary catarrhal jaundice it must be assumed that mild cholecystitis was present in addition. Cholelithiasis may date from catarrhal jaundice. Dilatation of the lower end of the common bile-duct has been thought to be a result of catarrhal inflammation, but it is probable that when this sequence is noted, the inflammation has been of considerable duration or intensity, or that there has been a gall-stone there. Just as the inflammation of the papilla may spread into the common bile-duct and cause chronic cholangitis, so the catarrhal process may extend into Wirsung's duct and set up acute or chronic pancreatitis. In extremely rare cases acute diabetes may follow what at the time appears to be catarrhal jaundice. Rose Bradford³ reported a case of this kind. This supports the view that pancreatitis may cause catarrhal jaundice.

In ordinary cases the **prognosis** is extremely good, there being no danger to life and very seldom any after-results of importance. On the other hand, what at first appears to be catarrhal jaundice may be the

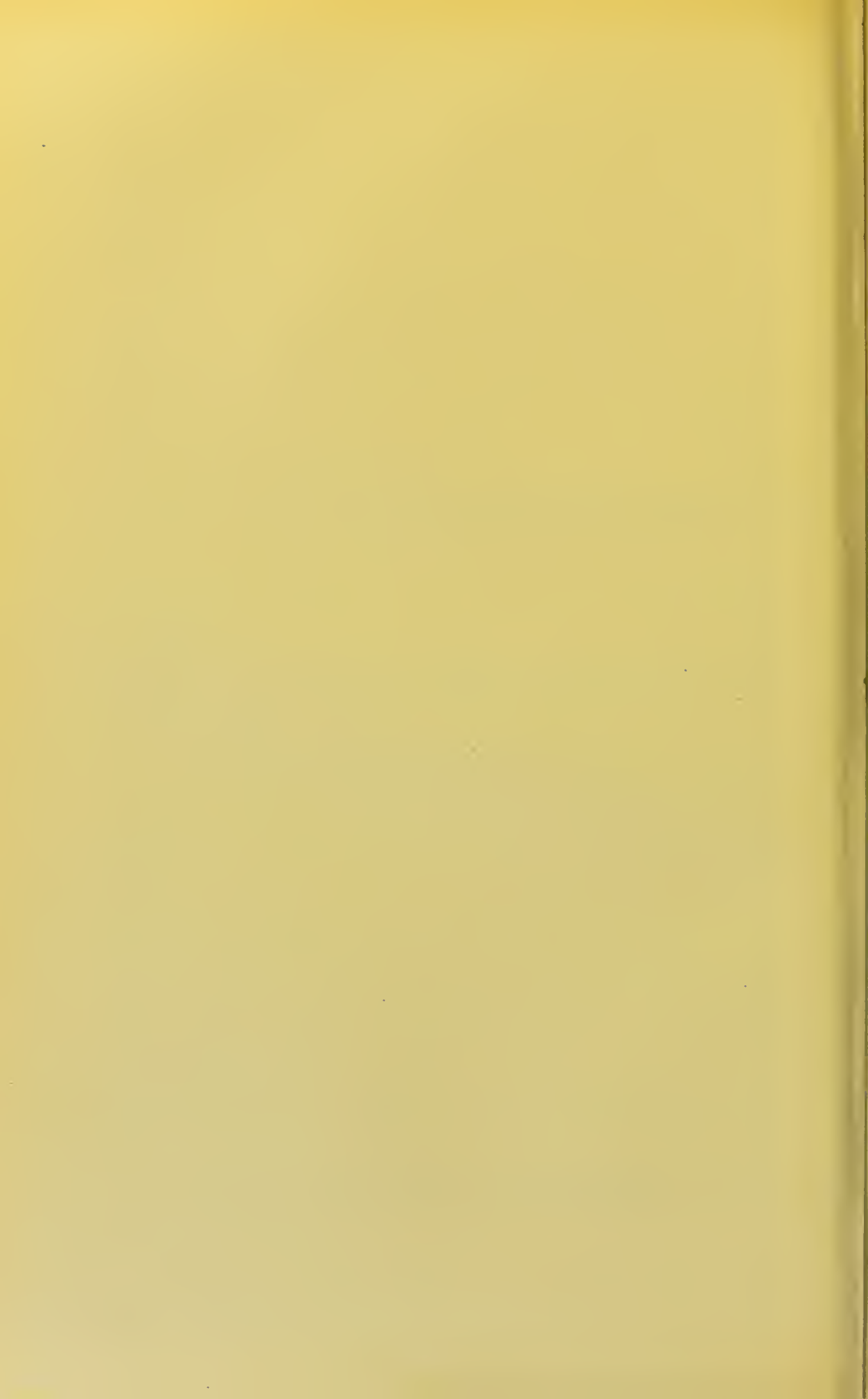
¹ Chauffard. *Traité de méd.* (Bouchard, Brissaud), 1902, v, 97.

² Robson. *Surg., Gynec., and Obst.*, Chicago, 1908, vi, 29.

³ Bradford, J. R. *Clin. Journ.*, Lond., 1907-8, xxxi, 76.

^/or(iii) possibly due to subacute hepatitis (Audibert).

Audibert. Rev. de méd., Paris, 1907, xxvii, 562.



initial manifestation of severe organic disease of the liver, such as malignant disease or acute yellow atrophy. It is, therefore, advisable to avoid giving a dogmatic prognosis in the early stages, if this can be done without creating alarm. In the vast majority the result of the case justifies a prognosis of complete and rapid recovery, given at the very outset; but in rare instances the clinical picture radically changes and nervous symptoms rapidly usher in coma and death from acute yellow atrophy, or, in less exceptional cases, the jaundice, instead of gradually disappearing, deepens into that of malignant obstruction of the common bile-duct. When catarrhal jaundice is prolonged, the prognosis alters, as the possibility of some grave cause of obstruction must be considered, but some of these protracted cases recover without any definite developments.

Diagnosis.—The presence of gastro-intestinal disturbance, vomiting, diarrhoea, loss of appetite, and dyspepsia before the onset of jaundice, the absence of severe constitutional disturbance and of pain, and the comparatively mild jaundice fading within a few weeks are the important points in the diagnosis. In some instances gastro-intestinal symptoms are absent and it is then difficult to eliminate at once more serious forms of jaundice; and it must be remembered that catarrhal jaundice may complicate grave hepatic disease. The age of the patient has some bearing, as catarrhal jaundice in late middle life may be the first indication of malignant disease involving the ducts. The duration and character of the jaundice are important; when jaundice lasts more than six weeks, the diagnosis of simple catarrhal jaundice should be seriously questioned, and some other cause sought for. Deep green or "black" jaundice excludes catarrhal jaundice. Several recurrent attacks point to the presence of a calculus in the common duct.

Cases of mild toxæmic jaundice, especially those with only slight fever and enlargement of the liver, are readily confused with catarrhal jaundice. In well-defined toxæmic or infective jaundice there are signs of general infection, such as fever, albuminuria, splenic and hepatic enlargement, but in the milder cases some of these manifestations may be absent and there is a transition to catarrhal jaundice.

The jaundice accompanying the presence of gall-stones in the common duct is much more prolonged than in catarrhal jaundice, and is usually characterised by periodic outbursts of fever, pain, and exacerbations in the degree of jaundice (*vide* p. 761). It may be preceded by biliary colic, but this is by no means always the case, and it may come on quite gradually. It occurs in older persons than catarrhal jaundice, especially in women.

Treatment.—In the early stage, while there is still some gastro-intestinal catarrh, it is important to treat this and to avoid irritation of the stomach by food; gastric disturbance should be allayed by bismuth combined with dilute hydrocyanic acid and bicarbonate of sodium, to which, if vomiting is troublesome, tincture of opium or chlorodyne may be added. The patient should be kept warm in bed, and for the first

day or so may with advantage be starved, but may take a fair amount of Vichy, Vals, Ems, Apollinaris, or hot water containing bicarbonate of sodium. Poultices or warm compresses to the upper part of the abdomen may be employed to relieve epigastric discomfort. Rest to the stomach is most important as a relapse is readily excited by food. Instead of absolute starvation whey may be given. Feeding should begin with peptonised milk or milk containing sodium citrate (grs. x. to the pint), beginning with $1\frac{1}{2}$ pints in the day and increasing it gradually. The bowels should be kept open either by enemas or by a small dose of calomel ($\frac{1}{2}$ –1 gr.) given at night and followed next morning by Carlsbad salts; or a pill of grey powder (1 gr.) may be taken three times daily, to which 1 to 2 grains of chalk may be added to prevent diarrhoea. Vigorous purgatives may set up or increase gastro-intestinal catarrh and should therefore be avoided.

When the gastro-intestinal catarrh has subsided, the bland milk diet should be relaxed, and thin clear soup, gruel, Benger's food, toast, soufflés, eggs, pounded fish, kedgeriee, chicken cream, and rice pudding given as the patient's condition allows. Fatty food, and especially liquid fat and melted butter, should be avoided. Minute doses ($\frac{1}{40}$ – $\frac{1}{20}$ gr.) of calomel, salicylate of bismuth, and salol are useful to inhibit intestinal fermentation; naphthalene tetrachloride, guaiacol, resorcin, and iodoform have been employed with the same object. Salicylate of sodium combined with urotropin should be given to increase the flow of bile and disinfect the bile-ducts. The action of the bowels must be maintained by the purgative waters or by salines, such as Epsom or Carlsbad salts, phosphate of sodium, and, if necessary, by blue pill. Rectal injections of water at 60–70° F. or even ice-cold to stimulate peristaltic action of the gall-bladder and so induce flushing of the bile-ducts by the bile have been recommended (Krull's irrigations). Massage to the liver has been advocated by Gilbert and Lereboullet,¹ and can be carried out at a spa by the liver douche.

During convalescence a tonic containing nux vomica is useful in improving the appetite and digestion. Dilute nitrohydrochloric acid is often given, but I prefer an alkaline medicine. Pruritus should be treated on the lines given on p. 567.

If the jaundice persists and there is no reason to suspect any grave underlying condition, such as malignant disease, the patient will probably receive benefit from a visit to a spa, such as Harrogate, Llandrindod Wells, Vichy, Neuenahr, Ems, Evian, Homburg, Carlsbad, Marienbad, or Bertrich.

¹ Gilbert et Lereboullet. *Gaz. hebd. de méd.*, Paris, 1901, vi, 913.





SUPPURATIVE CHOLANGITIS

Etiology.—The exciting cause of suppurative inflammation of the bile-ducts is a virulent infection ~~by the~~ bacteria which ~~have been found to give rise to this affection~~ ^{with} are mentioned on p. 673. The conditions and diseases which dispose to suppurative cholangitis are—(i) Local; and (ii) general.

(i) *The local conditions* are: Those which (a) diminish the resistance of the ducts, such as tumours, past inflammation, and (b) render infection more easy, such as biliary stagnation, gall-stones, rupture of hydatid cysts into the ducts, worms in the ducts. In biliary obstruction and stagnation micro-organisms which have got into the ducts either from the liver and general circulation (descending infection) or from the duodenum (ascending infection) have a better chance of multiplying and setting up inflammatory changes in the ducts, especially since, owing to dilatation, the ducts are probably less resistant than in health.

Cholelithiasis is the commonest antecedent of suppurative cholangitis; this was so in 18 out of 20 cases collected by L. Rogers.¹ The acute suppurative inflammation may supervene on old-standing infective cholangitis (*vide* p. 759) or may occur in a patient who has never had any manifest signs of cholelithiasis. When suppurative cholangitis supervenes on chronic catarrhal inflammation of the ducts, the more virulent infection may be supposed to be favoured by the diminished resistance of the ducts.

Rupture of hydatid cysts into the bile-ducts, though not nearly so frequent a cause of suppurative cholangitis as gall-stones, is a well-established factor. The presence of hydatid membranes in the ducts favours ascending infection from the duodenum, and it is probably to this that suppurative cholangitis is due. The subject of rupture of hydatid cysts into the bile-ducts is considered more fully on p. 418.

In hepatic abscess the inflammation may spread to the bile-ducts, or the abscess may open into the larger bile-ducts. Cholangitis may thus be secondary to hepatic abscess, and by giving rise to multiple foci of suppuration, renders a fatal issue almost certain.

Round worms and liver flukes may pass up the common bile-duct from the duodenum and carry with them micro-organisms. The ducts thus become infected, and suppuration, either diffuse or localised, of the ducts will readily result. When localised, the worm may be found in an abscess cavity in the liver (*vide* p. 683).

A tumour—papilloma or carcinoma—arising on the duodenal surface of the biliary papilla is not common, but is very prone to set up suppurative cholangitis; this depends on the following factors: (1) Obstruction to the outflow of bile and dilatation of the ducts diminish their resistance.

¹ Rogers, L. *Brit. Med. Journ.*, 1903, ii, 706.

Owing to ulceration and necrosis of the growth, the obstruction may intermit, and this intermission very probably favours infection from the duodenum. (2) The growth favours duodenal catarrh and thus renders ascending infection easy. (3) Stagnation of bile in the ducts favours infection.

The growth in the duodenum in the region of the papilla may be a papilloma or a carcinoma; in some instances it appears to the naked eye to be a papilloma, but microscopic examination shows invasion of the duodenal wall and therefore malignancy, as in the specimens in the Museums of Guy's and St. Bartholomew's Hospitals (*vide* p. 554).

Besides malignant disease of the duodenum, carcinoma of the ampulla of Vater and of the lower part of the common bile-duct may lead to suppurative cholangitis (*vide* p. 705). In malignant disease of the liver pressure on the ducts disposes to suppurative cholangitis.

A woman aged forty-four years in St. George's Hospital under the care of Sir I. Owen, with jaundice, was operated upon and found to have multiple growths on the surface of the liver. She had a febrile temperature until her death, one week later. The necropsy revealed primary carcinoma of the splenic flexure and secondary growths in the liver and in the portal fissure. The latter compressed the hepatic ducts. There was intrahepatic suppurative cholangitis. The gall-bladder was collapsed, had a secondary growth in its wall, but was not inflamed or occupied by gall-stones.

In rare instances an aneurysm of the hepatic artery may lead to multiple abscesses in the liver (Osler and Ross¹). The abscesses may be due to infective emboli, but they may also be the result of suppurative cholangitis. As bearing on the occurrence of suppurative inflammation of the ducts in association with aneurysm of the hepatic artery, it is interesting to note that Dujarier and Castaigne² have found that experimental ligature of the hepatic artery leads to stagnation of bile in the ducts and so favours infection.

(ii) *General Diseases Disposing to Suppurative Cholangitis.*—Suppurative cholangitis may occur after infective diseases attacking either the body generally or the alimentary canal.

General blood infections may set up inflammation of the small ducts in the liver in the same way that toluylenediamine, when employed experimentally, gives rise to a descending cholangitis. Micro-organisms or poisons may reach the liver by the blood-stream, and if the bile-ducts are previously damaged, micro-organisms may gain an entrance into the ducts and so set up cholangitis. Influenza and pneumonia have in rare instances been precursors of suppurative cholangitis. In both these diseases it is possible that the cholangitis might be an extension of inflammation from the duodenum, since there is a well-known gastro-intestinal form of influenza, and, in rare instances, pneumococic gastritis.

¹ Osler and Ross. *Canad. Med. and Surg. Journ.*, 1877, vi, 1.

² Dujarier et Castaigne. *Bull. Soc. Anat. Paris*, 1899, lxxiv, 329.





Suppurative cholangitis after influenza has been recorded by Mayo Robson¹ and Rémy²; in the latter case cultivations shewed a colon bacillus.

The diseases of the alimentary canal that may be followed by suppurative inflammation of the bile-ducts are typhoid fever and cholera.³ In typhoid affections of the biliary system the gall-bladder usually bears the brunt of the disease. It is very rare for suppurative cholangitis to occur independently of cholecystitis, though the two are often combined. Experimentally cholangitis has been set up by the injection of cultures of the comma bacillus into the bile-ducts of rabbits (Gilbert and Dominici⁴).

Bacteriology.—Various micro-organisms have been found to be associated with suppurative cholangitis. In some of the cases in which the colon bacillus has grown in the cultures it is not unlikely that other micro-organisms were present, but were crowded out by its vigorous growth. The chief organisms found are *Bacillus coli*, *B. typhosus*, *B. paratyphosus*, streptococci, staphylococci (albus, aureus), pneumococcus, comma bacillus. The colon, typhoid, and comma bacilli being motile, would be able to ascend the ducts from the intestine more readily than the non-motile streptococci and staphylococci. The *Bacillus aerogenes capsulatus*, which usually invades the tissues during the death agony, may, however, be present during life in the circulation, and may even be a primary infection.

In a case of multiple abscesses of the liver in carcinoma of the lower end of the common bile-duct a pure culture of *Bacillus aerogenes capsulatus* was obtained by Pratt and Fulton.⁵

Morbid Anatomy.—The mucous membrane of the ducts is swollen from inflammatory exudation and irregular from ulceration. The outer walls of the duct are also thickened and inflamed, and by extension there may be local peritonitis, which may lead to obliteration of the foramen of Winslow, or to suppurative pylephlebitis. The glands in the portal fissure are enlarged and soft. Possibly some of the areas of suppuration in the liver may arise as pericholangitic abscesses in connexion with the lymphatics. The suppurative process in the ducts may be associated with an empyema of the gall-bladder.

The liver is nearly always greatly enlarged, swollen, and of a greyish colour, with yellowish-green areas around the portal spaces. These foci are softening down into suppuration, and in early stages may, to the naked eye, resemble secondary new growths or even lymphadenoma. When the disease is fully developed, the bile-ducts may be enormously dilated so as to be as large as the small intestine, and have even been opened during laparotomy for supposed suppurative cholecystitis (Rogers⁶).

¹ Mayo Robson. Allbutt's *System of Medicine*, 1897, iv, 251.

² Rémy. *Congrès franç. de chir.*, 1896, x, 485.

³ Galliard. *La Choléra*, Bibliothèque Charcot-Debove, 1894.

⁴ Gilbert et Dominici. *Compt. rend. Soc. Biol.*, Paris, 1894, 10. s., i, 38.

⁵ Pratt and Fulton. *Boston Med. and Surg. Journ.*, 1900, cxlii, 599.

⁶ Rogers, L. *Brit. Med. Journ.*, 1903, ii, 706.

The suppurating ducts may terminate in small abscesses on the surface of the liver, somewhat resembling the condition of the lung in acute bronchiectasis. Numerous biliary abscesses may be scattered throughout



FIG. 93.—Microscopical appearances of the liver in suppurative cholangitis. There are numerous abscess cavities surrounded by condensed fibrous tissue, which appears more darkly stained. It is impossible to distinguish the bile-ducts from the branches of the portal vein, since both are involved. (Photomicrograph by Dr. H. Spitta. Low magnification.)

the liver, both on the surface and in its substance, and adjacent abscesses may run together and form a confluent or areolar abscess which shews fibrous septa. On the other hand, there may be a single localised abscess, or only a few small abscesses formed of ampulla-like dilatations of the



ends of the ducts. The pus is often bile-stained, and may contain soft, calculous matter like brown mud. In the substance of the liver abscesses may form outside the ducts, possibly in the lymphatics, and suppuration may extend into the branches of the portal vein, causing pylephlebitis and diffuse suppuration of the portal spaces.

The suppuration may spread into Wirsung's duct and set up suppurative pancreatitis, and, by further extension of infection to the peritoneum covering the pancreas, a local abscess in the lesser sac of the peritoneum. Pancreatitis due to gall-stones in the common duct is referred to on page 764. Suppuration may spread from the pancreas into the portal vein and set up pylephlebitis.

The suppurating bile-ducts may leak into the peritoneum and cause general peritonitis or a local peritoneal abscess. Abscesses on the convex surface of the liver may perforate the diaphragm and cause an empyema or broncho-biliary fistula; abscesses on the under surface may open into the colon or set up a perinephric abscess (Rogers).

Microscopically the larger portal spaces are dilated, and relics of their fibrous tissue are visible, but it may be difficult to distinguish the remains of the large bile-ducts from those of the portal veins, since both may be involved in the same suppurative process. The walls of the ducts may be destroyed and replaced by small cells which extend into the surrounding liver substance. There may be comparatively well-formed fibrous tissue from chronic pericholangitis, but the chief feature is diffuse small-celled infiltration. In places the liver cells can barely be recognised, and the condition is that of a commencing abscess.

Clinical Picture.—The onset may be insidious. The patient is feverish, has rigors, anorexia, nausea and vomiting, marked prostration, and loss of flesh. The temperature may be only moderately raised and may even be subnormal in the later stages. The liver, which is generally much enlarged and tender, progressively increases in size as the disease goes on; in some instances, however, little or no enlargement can be made out. It is usually smooth but may be irregular. The spleen is enlarged. Jaundice, when present, depends not so much on the cholangitis as on gall-stones, worms in the ducts, rupture of hydatid cysts into the ducts, and new growths of the biliary papilla and the region of the ampulla of Vater. But in the absence of such local conditions suppurative cholangitis may run its course without jaundice.¹ This is difficult to explain; but possibly the absence of jaundice may depend on occlusion of the hepatic lymphatics, which should carry the bile into the general circulation, by the inflammatory changes. In the following case there was very slight jaundice:

A man aged twenty-nine years was admitted to St. George's Hospital in an extremely grave condition, with a large tender liver, an anaemic, sallow complexion, slight ascites, and a history that two weeks ago he had had fever and

¹ *Vide* Gilbert et Lereboullet. "Les Angiocholites anictériques," *Bull. et mém. Soc. méd. d. hôp. de Paris*, 1900, 3. s., xvii, 477.

jaundice. Two and a half years ago he had had appendicitis. The temperature was subnormal. At a consultation various opinions were expressed, such as pylephlebitis secondary to appendicitis, suppurative cholangitis associated with calculi, abscess, and rapid new growth of the liver. The following day an exploratory operation was performed, and a nodule, which might have been either new growth or early inflammatory change, was cut into. Microscopic examination shewed altered liver cells. The patient died two days later. At the necropsy the liver (7 pounds) shewed suppurating areas around the bile-ducts; the extrahepatic bile-ducts contained mucus. There were no calculi in the gall-bladder. The portal vein and vermiform appendix were normal. The spleen was large and soft, weighing 17 ounces.

Pain may be due to perihepatitis set up by suppuration in the ducts under the capsule, and is worse on respiration and on movement. Colicky pain may be caused by factors underlying the acute infection, such as gall-stones, the rupture of hydatids into the ducts, or worms in the ducts. Pseudo-gall-stone colic may also occur when malignant disease obstructs the ducts. In some instances pain is entirely absent.

Septic absorption which causes the severe constitutional symptoms may lead to diarrhoea and albuminuria. There is leucocytosis, and blood-cultures shew micro-organisms. From local or general peritonitis, secondary to leakage of abscesses on the surface of the liver, abdominal distension may come on before death.

Complications.—In addition to local (such as subphrenic abscess or suppuration in the lesser sac of the peritoneum) or general peritonitis from leakage or rupture of the suppurating areas, general haemic infection may occur. Pus and micro-organisms may pass into the hepatic veins and so reach the lungs and give rise to pyaemic abscesses, pleurisy, and empyema. Empyema, however, may be secondary to subphrenic suppuration and due to the spread of infection through the diaphragm. When the micro-organisms have got into the general circulation, the joints and meninges may be affected, and infective endocarditis may be induced in the same way.

Duration.—As suppurative cholangitis may supervene in chronic catarrhal cholangitis, it is difficult to fix the duration with accuracy. In most cases in which the disease comes on acutely it lasts about three weeks. In exceptional instances in which the suppurating ducts have discharged into the colon or bronchus, the course of the disease is much prolonged. Thus, Rogers¹ describes cases which lasted eighteen and six months respectively. The importance of drainage in the duration of the disease is shewn by the prolonged course of broncho-biliary fistulae, most of which are due to suppurative cholangitis.

Diagnosis.—Fever and grave constitutional disturbance in a patient whose liver progressively increases in size and who has had symptoms pointing to gall-stones are the features of importance. Jaundice is not constant, but its presence is in favour of suppurative cholangitis as against suppurative pylephlebitis and tropical abscess.

¹ Rogers, L. *Brit. Med. Journ.*, 1903, ii, 706.



The differential diagnosis must be made from intermittent hepatic fever due to gall-stones, from two other forms of intrahepatic suppuration—pylephlebitis and tropical abscess, from new growth associated with fever, and from acute cirrhosis with jaundice.

In *intermittent hepatic fever* there are periodic attacks of fever, pain, and intensification of jaundice, but in the intervals the patient is comparatively well (*vide* p. 762). In suppurative cholangitis the fever is continuous: jaundice is not so prominent, and the patient's general condition is much graver.

Pylephlebitis is accompanied by the same general symptoms and hepatic enlargement as suppurative cholangitis. Jaundice is more frequent, appears earlier, and is more marked in cholangitis, whilst splenic enlargement is more often prominent in suppurative pylephlebitis. According to Libman¹ blood-cultures are negative in pylephlebitis and positive in cholangitis. It must be remembered that these two conditions may be combined. In *malaria* examination of the blood should shew parasites, and in cholangitis a polymorphonuclear leucocytosis. In *tropical abscess* there is often a history of dysentery and there may be fluctuation or local bulging with oedema of the chest-wall. In cases in which the abscess is deeply situated the diagnosis is difficult. The history of past dysentery or gall-stones is in favour of single abscess or cholangitis respectively; jaundice, if present, makes cholangitis more probable. But in case of doubt, the rarity of suppurative cholangitis and the relative frequency of abscess must have their due weight. Very rapid *new growth* in the liver accompanied by fever and jaundice may closely resemble suppurative cholangitis; in fact some cases of carcinoma involving the ducts shew suppurative cholangitis. In the absence of evidence of new growth, such as a palpable tumour, the diagnosis may be possible only when the liver is freely exposed. In cases of *acute cirrhosis* with fever, jaundice, and enlargement and tenderness of the liver the resemblance to suppurative cholangitis is very considerable. In this form of cirrhosis there are usually a marked alcoholic history, splenic enlargement, and haematemesis, and the constitutional symptoms are less severe than in suppurative cholangitis.

The **prognosis** depends on the course of the disease; if it remains limited to the large ducts or is operated on early, before it has spread to the liver or pancreas, recovery may occur; probably some cases of empyema of the gall-bladder began as suppurative cholangitis, the original lesion having passed away. If it invades the liver and sets up multiple abscesses and diffuse suppuration of the portal spaces, a fatal termination is inevitable; but there may be only a single local area of suppuration in the liver and the outlook is then much better. In addition to its course and complications, much depends on early operation and free drainage. When a broncho-biliary fistula or a communication between the biliary abscess and another hollow viscus, such as the colon or pelvis of the kidney, forms, the free drainage greatly prolongs life and a cure may

¹ Libman. *Am. Journ. Med. Sc., Phila.* 1908, cxxxvi, 548.

even result. These cases with fistulae in fact differ so much from the rapid course of suppurative cholangitis that they are usually considered as a separate condition.

The proper treatment is surgical, and consists in obtaining free drainage for the pus; this may be done by opening the dilated ducts, by cholecystotomy, or by opening biliary abscesses on the surface of the liver.

Medical treatment is only palliative, but it may be combined with surgical treatment and then be of distinct use. Salicylate of sodium combined with urotropin, to wash out and disinfect the ducts, should be given.

CHRONIC CATARRHAL CHOLANGITIS

Chronic infective or catarrhal cholangitis may be divided into two forms: (i) That associated with and largely due to cholelithiasis, and (ii) that due to other causes. The form associated with the presence of a gall-stone in the common bile-duct is so intimately related to cholelithiasis that it is described in connexion with that disease (*vide* p. 759). Non-calculous chronic catarrhal cholangitis will be described under two headings: (A) of the extrahepatic bile-ducts, and (B) of the intrahepatic bile-ducts.

(A) **Non-calculous Chronic Catarrhal Cholangitis of the Extra-hepatic Ducts.**—It may depend on chronic gastro-duodenal catarrh, such as is seen in drunkards. It may occur in the course of malignant disease of the liver or of the bile-ducts, and in the latter condition is more likely to supervene when the growth is at the biliary papilla. Suppuration in the liver or the rupture of hydatid cysts into the bile-ducts may set up cholangitis which may be catarrhal at first, but is more likely to become suppurative. Infectious diseases, such as typhoid, influenza, pneumonia, may play some part in the production of chronic catarrh of the bile-ducts. Acute cholangitis may occur in enteric fever and influenza, and probably may leave behind chronic catarrh. How often they may set up slight chronic catarrh without any previous acute inflammation it is difficult to say. In some cases of prolonged catarrhal jaundice¹ which, after hanging fire for weeks and months with intermissions and exacerbations, eventually clear up completely, there may be an underlying chronic inflammation of the common duct.

Clinical Aspect.—When supervening on acute catarrh the jaundice remains and may arouse the suspicion of malignant disease or of an impacted calculus in the common duct. The chronic jaundice leads to some wasting from malnutrition. It varies in intensity from time to time, becoming more marked after attacks of fever and pain. The general features are those of chronic relapsing jaundice, and are in miniature

¹ *Vide* Dieulafoy. *Semaine méd.*, Paris, 1888, viii, 270.



the same as those of intermittent hepatic fever (*vide* p. 759). The inflammation may spread upwards to the liver, and in very rare instances be followed by acute yellow atrophy; or suppurative cholangitis may develop.

The *diagnosis* of chronic catarrhal inflammation of the larger bile-ducts from hypertrophic biliary cirrhosis with chronic jaundice turns on the absence of the marked hepatic and splenic enlargement.

From a gall-stone in the common duct with chronic infective cholangitis the diagnosis is very difficult, inasmuch as the two conditions are much the same, except for the presence of a gall-stone. I believe that non-calculous cases react much better than calculous cases to urotropin and salicylates. In cholelithiasis with infective cholangitis there is more pain, and the attacks of intermittent hepatic fever are better marked, but not uncommonly there is no history of cholelithiasis, and a differential diagnosis between these two closely allied conditions may not be justified. It is so much commoner to find a gall-stone in the lower end of the common duct in chronic catarrhal or infective cholangitis, that this condition should be diagnosed in any doubtful case.

Treatment.—The diet should be simple, and milk should form a large proportion of the food. Irritating food and alcohol must be forbidden. Calomel and saline purges should be given to prevent constipation and minimise gastro-intestinal catarrh; for the latter purpose alone calomel should be given in minute doses ($\frac{1}{20}$ gr.) three or four times daily, and urotropin and salicylates and plenty of water so as to disinfect and flush the bile-ducts. Benefit will result from a visit to a spa, such as Harrogate, Llandrindod, Leamington, Bath, Vichy, Neuenahr, Homburg, Carlsbad.

In prolonged cases in which no benefit follows medical and spa treatment, the question of operation with a view to draining the ducts should be considered. This course is also indicated by the difficulty of eliminating the presence of a calculus in the common duct. Lejars¹ and Quénu² report cases cured by operation. Some of the cases regarded as hypertrophic biliary cirrhosis, in which cholecystotomy and drainage have been followed by cure may have been examples of chronic infective cholangitis.

Guillot³ gives a list of 13 cases of chronic hypertrophic biliary cirrhosis or closely allied conditions in which cholecystotomy and drainage were performed, mainly by Delagénère. Recovery followed in 10.

(B) **Non-Calculous Chronic Catarrhal Cholangitis of the Intra-hepatic Bile-Ducts.**—Our knowledge of chronic cholangitis of the intra-hepatic bile-ducts (or angiocholitis) is very deficient. It may be assumed that bacteria or poisons conveyed to the liver, either by the portal vein or by the hepatic artery, may give rise to inflammation of the intrahepatic

¹ Lejars. *Med. Week*, Paris, 1897, v, 139.

² Quénu. *Ibid.*, 1897, v, 163.

³ Guillot. *Gaz. hebdomadaire de méd.*, Paris, 1902, vii, 49.

ducts ; and that cholangitis complicates diseases of the liver, such as portal cirrhosis, chronic venous engorgement, hepatitis, and malignant growths. Chronic cholangitis occurs in hypertrophic biliary cirrhosis with chronic jaundice, but all cases of chronic catarrh of the intrahepatic ducts do not conform to the type of Hanot's disease, though the conditions are allied. The small ducts shew proliferation of the lining epithelium, which may block up the lumen ; there may be some dilatation of the small bile-ducts, and there is pericholangitic fibrosis.

The following conditions have been ascribed to chronic angiocholitis, but their pathological nature requires confirmation.

Klippel and Vigouroux¹ described a case of chronic cholangitis with hepatic insufficiency, diarrhoea, no jaundice or enlargement of the spleen, in which signs of acromegaly developed. The authors suggest that this was due to hepatic insufficiency in the same way that clubbed fingers develop in hypertrophic biliary cirrhosis. The liver shewed angiocholitis and fibrosis of the portal spaces. Lereboullet² described a somewhat similar condition under the name meta-icteric splenomegaly. Jaundice due to cholangitis occurs first, and subsequently as it recedes, the spleen becomes enlarged. The enlargement of the spleen is supposed to be due to passive venous engorgement produced by pressure on the branches of the portal vein by sclerosing cholangitis.

Cases thought to be due to chronic catarrhal inflammation of the small intrahepatic ducts should be treated with plenty of water and occasional courses of salicylate of sodium, combined with urotropin, so as to wash out the ducts and remove catarrh. Minute doses of calomel ($\frac{1}{20}$ gr.) may be given two or three times a day to minimise intestinal fermentation, and the bowels should be kept freely open and the diet should be simple and nourishing. Alcohol should be forbidden. Spa treatment on the same lines as in chronic catarrhal cholangitis of the larger ducts may be adopted.

PERICHOLANGITIS

Pericholangitis may be divided into : (a) Extrahepatic, affecting the larger bile-ducts ; and (b) intrahepatic. Extrahepatic pericholangitis may accompany changes in the larger ducts, but is entirely subordinate to that condition.

Intrahepatic Pericholangitis.—This is chiefly of pathological interest, since it either occurs as part of other morbid lesions or has no definite clinical associations. It is met with under different conditions and may be acute, as in suppurative cholangitis, of which it forms part, or it may be chronic.

¹ Klippel et Vigouroux. *Presse méd.*, Paris, 1903, i, 245.

² Lereboullet. *Semaine méd.*, Paris, 1903, xxiii, 180.



Acute pericholangitis cannot be recognised apart from acute inflammation in the portal spaces, such as suppurative cholangitis or pylephlebitis, to which it is, as far as is known, practically always secondary.



FIG. 94.—Naked-eye appearance of a section of liver with white material due to chronic pericholangitis. There was also secondary pylephlebitis.



FIG. 95.—Photomicrograph of the white material occupying a portal space. It is composed of granulation tissue. The space at the top represents the remains of the portal vein, which in this instance was destroyed by secondary suppurative pylephlebitis.

It is, however, quite conceivable that an acute inflammation of the lymphatic vessels around the bile-ducts might occur independently of cholangitis. It might be set up by an abscess in the liver.

Chronic pericholangitis occurs in several conditions described elsewhere ; thus, in hypertrophic biliary cirrhosis and in gall-stone obstruction with infection of the ducts there is fibrosis around the smaller bile-ducts from extension of inflammation in their interior.

In a case of enormous dilatation of the intrahepatic bile-ducts in which the liver was like a hydronephrotic kidney, there was extensive chronic pericholangitis (Raynaud and Sabourin¹).

In the condition described as tuberculous cavities in the liver the tuberculous process begins in the loose tissue surrounding the bile-ducts —tuberculous pericholangitis.

Pericholangitis, which is not an entirely subsidiary part of cholangitis, is seen in very rare instances. To the naked eye the portal spaces are occupied by white material (Fig. 94) which has a close resemblance to tubercle. Strangeways Pigg and I² described a case, and Morley Fletcher³ has since given an account of another. In the first it appeared probable that catarrhal cholangitis had set up chronic pericholangitis, but Fletcher took the view that the pericholangitis was primary. In our case there was secondary suppurative pylephlebitis ; in Fletcher's the portal vein was healthy. The inflammation involves the portal lymphatics ; in our case the glands in the portal fissure were much enlarged, and to the naked eye there was some resemblance to lymphadenoma. The white material in the portal spaces is composed of granulation tissue in various stages of development (Fig. 95), and in these two cases were certainly not tuberculous. It contained numbers of bile-ducts, many of which were proliferating and dilated. According to Amet and Carnot⁴ the elastic fibres spreading out from the ducts may be increased in amount.

Clinically, these cases did not present any characteristic features. In Morley Fletcher's case there was bronchiolectasis, and in our case the patient had advanced renal disease and several attacks of haemorrhage from the bowel. In neither was there jaundice ; this can to some extent be explained by supposing that blocking of the lymphatics prevented the absorption of bile by the lymph channels.

PARASITIC AFFECTIONS OF THE BILE-DUCTS

Ascaris Lumbricoides.—A round worm in the duodenum may work its way into the biliary papilla and common bile-duct and give rise to biliary obstruction and infection of the ducts. Cases have been described in which jaundice has disappeared after the passage of a bile-stained

¹ Raynaud et Sabourin. *Arch. de physiol. norm. et path.*, Paris, 1879, 2. s., vi, 37.

² Rolleston and Strangeways Pigg. *Journ. Path. and Bacteriol.*, 1898, v, 221.

³ Morley Fletcher. *Trans. Path. Soc.*, Lond., 1901, lii, 193.

⁴ Amet et Carnot. *Arch. de méd. expér. et d'anat. path.*, Paris, 1906, xviii, 763.

Resection of the colon
Chic. de 1913, Vol. 2, p. 514
des colon
Cancer
Le cancer du colon

Hertelome (Lyon chir., 1922, 47 68)
Collected 61 cases in which
operation removed the tumor
from the bile ducts or near

round worm shewing a constriction (Ebstein,¹ Hilliary²); and it has been reasonably assumed that in some instances the head of the worm has temporarily blocked the lower end of the bile-duct. Mertens³ collected 48 cases of round worms in the bile-ducts, and Sick⁴ brought together 64 cases. From the frequency of ascarides in the young it is natural that some of the cases of bile-duct infection are in children. The worms dilate the bile-ducts, carry micro-organisms with them, and, by infecting the bile-passages, give rise either to suppurative cholangitis or to single or multiple abscesses in the liver.

Roud⁵ described a case with streptococci and colon bacilli in the hepatic abscesses, which also contained gas.

In 5 of Merten's cases, gall-stones were associated with the presence of round worms. Hanot⁶ regards the cholelithiasis as due to the infective agency of the worms. In his own case Mertens believed that the passage of a calculus assisted the entrance of the worm by dilating the passage.

The following case recorded by John Davy⁷ is one of the earliest and illustrates the condition well. A Maltese boy aged two years who died from dysentery, was found to have numerous round worms in the stomach, small intestine, colon, and liver. The common and hepatic ducts were distended with worms, and there were several abscesses in the liver containing worms.

A specimen (No. 533) in the Cambridge Pathological Museum shews the bile-duct distended with *Ascaris lumbricoides*. The patient was a child. The duct was so tensely distended that jaundice must have been produced, though there is no history of the case.

The *clinical features* are enlarged liver, jaundice, fever, attacks of biliary colic, and, in a word, those of infective cholangitis with biliary obstruction. In only 2 of 48 cases collected by Mertens was a diagnosis made during life. The diagnosis depends on finding the worms or their ova in the dejecta; otherwise the cases are likely to be regarded as due to gall-stones.

Treatment.—Santonin should be given if the presence of round worms is suspected. In the presence of signs of infection of the common duct the duct should be cut down upon and drained. ~~In a case diagnosed as a calculus in the common duct recovery followed choledochotomy (Neugebauer⁸).~~

Distomiasis.—Several species of distomidae may be met with in the bile-ducts of the liver in man.

¹ Ebstein. *Deutsches Arch. f. klin. Med.*, 1904, lxxxi, 543.

² Hilliary. *Journ. Am. Med. Assoc.*, Chicago, 1905, xlv, 1655.

³ Mertens. *Deutsche med. Wchnschr.*, 1898, xxiv, 358.

⁴ Sick. Inaug. Dissert., Tübingen, 1901. Quoted by Neugebauer. *Arch. f. klin. Chir.*, 1903, lxx, 584.

⁵ Roud. *Thèse de Lausanne*, 1896.

⁶ Hanot. *Arch. gén. de méd.*, Paris, 1896, clxxvii, 74.

⁷ Davy, J. *Diseases of the Army*, p. 423, 1862. This specimen is in the Museum of the Royal Army Medical College, Millbank (Series xxix., No. 131), and is figured in 3rd Fasciculus of Drawings of Specimens in Army Medical Museum, Chatham, Plate II. Printed by Taylor, London, 1838.

⁸ Neugebauer. *Arch. f. klin. Chir.*, 1903, lxx, 584.

Fasciola hepatica (*Distomum hepaticum*) or liver-fluke is common in sheep, and gives rise to the disease known as sheep-rot, which has proved so disastrous to so many sheep-farms. In very rare instances men have become infected from taking water or vegetables contaminated with the dejecta of sheep suffering from the disease. ~~Out of 24 reputed cases Ward¹ considers that 14 are authentic.~~ Infection with *Fasciola hepatica* may arise in this country, which is not the case with the other varieties of distoma. Invasion of the ducts by distoma is much commoner in tropical countries, such as China, Japan, and India.

Opisthorchis sinensis (~~*Distomum sinense*~~) is found in India, China, Japan, and Tonkin. In Japan 20 per cent of the inhabitants in certain low-lying districts are affected; they suffer from diarrhoea, ascites, cachexia, and eventually die (Baelz²). *Dicrocoelium lanceatum* (*Distomum lanceolatum*) and *Opisthorchis noverca* (*Distoma conjunctum*) have in extremely rare instances been met with in the bile-ducts of human beings, but are of no real pathological importance.

Morbid Anatomy.—The distomes cling by their suckers to the mucous membrane of the bile-ducts, which become dilated, shew epithelial proliferation and small papillomas, and contain mucus and the ova of the worms. Cystic dilatations varying from the size of a hazel-nut to a walnut may form in the course of the ducts. There is inflammation with an accumulation of eosinophil cells around the bile-ducts. Suppuration may occur in the dilated bile-ducts. The liver is enlarged and may shew perihepatitis.

Clinical Aspect.—Though sometimes the worms remain latent, some of the following symptoms and signs may be expected: Hepatic pain and enlargement, jaundice, gastro-intestinal disturbance, vomiting, diarrhoea or constipation, fever, enlargement of the spleen, ascites, oedema of the feet, and anaemia. \wedge The cases may terminate as suppurative cholangitis or abscess of the liver, and the prognosis is therefore bad. The diagnosis depends on the detection of the ova in the stools. The treatment consists in giving vermicides, such as Filix mas and purgatives. When there are signs of suppurative cholangitis, the common bile-duct should be opened.

Psorospermiosis.—The invasion of the bile-ducts of the rabbit by the *Coccidium cuniculi* is extremely common, and leads to the production of papillomatous growths from the mucosa of the dilated ducts. On section, the liver shews white, caseous areas closely resembling tubercles to the naked eye. These appearances have been often described, and reference may be made for a detailed account of the parasite and its effects to Delépine's³ paper. Sometimes, as the result of secondary infection, acute inflammation is set up in the ducts and the mucous membrane becomes replaced by granulation tissue—psorospermial cholangitis.

Psorospermial invasion is very rare in the human liver, but it has

¹ Ward. *Brit. Med. Journ.*, 1911, i, 930.

² Baelz. *Berlin. klin. Wchnschr.*, 1883, xx, 234.

³ Delépine. *Trans. Path Soc.*, Lond., 1890, xli, 348.

In 1916 TAUFFLIER collected 56 cases mainly from neoplasms.

Maurry and Pelissier accept 39 reported cases including their own which was the 4th cured by operation.

Eosinophilia, usually above 20 per cent., ^{occurs} ~~is characteristic~~ ^{is not present} in all cases (Maurriac).

TAUFFLIER. Thèse de Lyon, 1916

Maurry E. et Pelissier, R. Presse méd., Paris 1924,

213.

MAURRIAC, P. Ann. de méd., Paris, 1922, XI, 420.

In a male infant 8 days old
who died from umbilical
haemorrhage with deep jaundice,
the bile ducts contained protozoa obstructed.
(Mouchet) Dobell in a critical review
accepts 3 cases only of hepatic infection in
man, those of Gubler, Dressler and
Schoeck.

Mouchet. Arch. de méd. expér. et d'anat. path., 1911, XXIII, 115

Dobell, C. Parasitology, Cambridge, 1919, xi, 164

been more often described in the liver than in any other internal organ of the human body. McFarlane¹ collected 20 cases of human psorospermiosis, and, omitting supposed psorospermial affections of the skin, such as Darier's disease, found that the liver was affected 11 times, the intestines 5 times, the kidneys twice, and the pleura and spleen once each.

A case of calcification of a psorospermial tumour removed during life from a patient who was thought to have a calcified gall-bladder is put on record by Carrel.² In Silcock's³ case there was considerable enlargement of the liver,

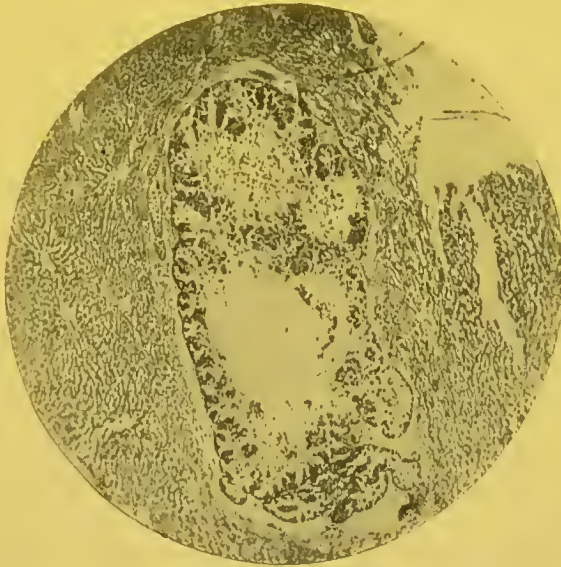


FIG. 96.—Section of rabbit's liver under a low power, with papillomatous growths in the dilated bile-duct due to the irritation of psorosperms. (Photomicrograph by Dr. S. G. Penny.)

which weighed 83 ounces. The spleen and intestines were also affected, and psorosperms were cultivated for two months. Podwysoski⁴ reported 4 cases, A

It is, however, not unlikely that some cases have been overlooked and the lesions regarded as caseous tubercle, and that a microscopic examination would have revealed the presence of psorosperms. The coccidia are taken in food, multiply in the stomach, and invade the common bile-duct.

Clinical Aspect.—In the human subject the symptoms are obscure. Some cases have shown fever, enlargement and tenderness of the liver without jaundice, and prostration. In rabbits eosinophilia has been observed (Federici⁵), and would be anticipated in man.

¹ McFarlane. *Journ. Applied Microscopy*, Rochester, 1898, i, 41.

² Carrel. *Lyon méd.*, 1900, xciii, 89.

³ Silcock. *Trans. Path. Soc.*, Lond., 1890, xli, 320.

⁴ Podwysoski. *Centralbl. f. Bakt. u. Parasit.*, 1889, vi, 41.

⁵ Federici. *Riv. crit. di clin. med.*, 1902.

Porocephalus Constrictus.—*Syn.* *Pentastomum constrictum*.—This parasite gains entrance to the alimentary canal, and, reaching the liver, gives rise to cysts, especially in the neighbourhood of the falciform ligament, which are thought to be dilated bile-ducts. The cysts contain clear fluid and a single coiled-up parasite which may be alive at the time the liver is examined after death. The walls of the cyst are composed of firm fibrous tissue and have a great tendency to undergo calcification. The peritoneum in the neighbourhood of the cysts may shew considerable inflammation, and infection of the lungs may occur. It is remarkable

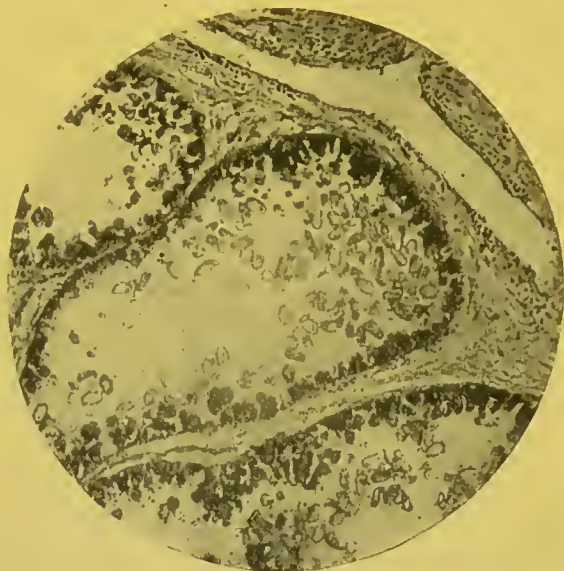


FIG. 97.—The same section under a higher power, shewing the coccidia loose in the dilated bile-duct. (Photomicrograph by Dr. S. G. Penny.)

that though the parasite gives rise to inflammation of the peritoneum and lungs, it does not appear to irritate the intestines and liver.

Cysts containing the parasite have been observed in the liver by Pruner,¹ Aitken,² Giard,³ Chalmers,⁴ ~~and~~ Thiroux.⁵ It is said to occur only in negroes, but this is not correct, as there is a specimen of a liver with five cysts containing the parasite, in the museum at the Royal Army Medical College, Millbank (Series xxix. No. 133), taken from an English soldier who died of spinal caries. Fibrosed cysts containing the larvae of *Linguatula rhinaria* have often been found on the surface of the liver.

Balantidium coli.—*Synonym:* *Paramoecium coli*.—This parasite is very common in the colon of the pig, and has been found in the intestines of man in association with diarrhoea. In the following unique case the parasite was found in the liver of man :

¹ Pruner. *Krankheiten des Orients*, Erlangen, 1847, S. 245.

² Aitken. *Science and Practice of Medicine*, Lond., 1868, i, 650.

³ Giard. *Compt. rend. Soc. Biol.*, Paris, 1896, 10. s., iii, 469.

⁴ Chalmers. *Lancet*, 1899, i, 1715, 1729.

⁵ Thiroux. *Compt. rend. Soc. Biol.*, Paris, 1905, 10. s., ii, 78. ?

1) Sambon, Löhleim, MacFie and Johnston

Sambon. Journ. Trop. Med. and Hyg., 1910, 1913
Löhleim. Arch. f. Schiffs- und Tropen-Hyg., 1912, xvi,
MacFie and Johnston. Lancet, Lond., 1913, ii, 1387.

In the liver of a man aged fifty-nine years Russell and Buzzard¹ found a dozen cysts the size of peas containing living paramoecia. The cysts, which had firm fibrous walls, were probably derived from the bile-duets and due to the irritation set up by paramoecia which had travelled up the bile-duets from the duodenum. The cysts did not shew any papillary growths resembling those in psorospermiosis of the liver. As the patient died from gastric carcinoma, it is not improbable that absence of HCl in the gastric juice allowed these organisms to develop in the stomach. No proof of this, however, is forthcoming, as the vomit was not examined.

INNOCENT TUMOURS OF THE BILE-DUCTS

INNOCENT tumours of the bile-duets are rare.

Papilloma.—Very few examples of papilloma of the larger extrahepatic bile-duets are on record, but probably the condition is not so exceptional as the number of published cases would suggest. Some of the cases described as malignant, but not examined microscopically, may have been innocent.

Chappet² speaks of a case of carcinoma, but states that the growth developed at the expense of the mucosa, which was not ulcerated, and that the other coats of the duct were little or not at all affected, so that it may have been an innocent papilloma.

Extensive mucoid change in papillomas of the bile-duets might produce a condition such as that described by Wilks and Moxon³ in a child aged four years whose common bile-duct, dilated to the size of its head, contained pendulous myxomatous growths with muscular fibres in them. The small fatty tumours described by Wardell⁴ as obstructing the cystic and common bile-duets might also be regarded as originally papillomas of the bile-duets, which subsequently underwent myxomatous degeneration and then, from bile-staining, took on a yellowish tinge, suggesting fat; for no microscopic examination appears to have been made. Devic and Gallavardin⁵ quote similar cases of lipomas arising from the mucosa of the bile-duets recorded by Ehrmann and by Dickmann. As submucous lipomas occasionally occur in the intestines, it is quite possible that they may be found in the bile-duets.

A papillomatous growth, from the inside of the common bile-duct, was removed by Sir W. Bennett from a woman at St. George's Hospital. It was close to a gall-stone that had been impacted for two months.⁶ It was a branching papilloma, composed of a basis of fibrous tissue covered over by columnar

¹ Russell and Buzzard. *Trans. Path. Soc.*, Lond., 1899, 1, 149.

² Chappet. *Lyon méd.*, 1894, lxxvi, 146.

³ Wilks and Moxon. *Pathology*, p. 485, 3d ed., 1889.

⁴ Wardell. *Lancet*, Lond., 1869, ii, 407.

⁵ Devic et Gallavardin. *Rev. de méd.*, Paris, 1901, xxi, 570.

⁶ Rolleston. *Trans. Path. Soc.*, Lond., 1894, xlv, 83.

epithelium (Fig. 98). In places the connective tissue had undergone mucoid degeneration. The after-history of the patient, however, rather suggested malignant disease (*vide* p. 690). A papilloma arising from the inside of the common duct one inch above the biliary papilla was considered by Eve¹ to have obstructed the duct in a valvular fashion and so to be responsible for cystic dilatation of the common duct.

The papillomatous growths in rabbits' intrahepatic bile-ducts, due to the irritation of psorosperms, are extremely common, but a similar

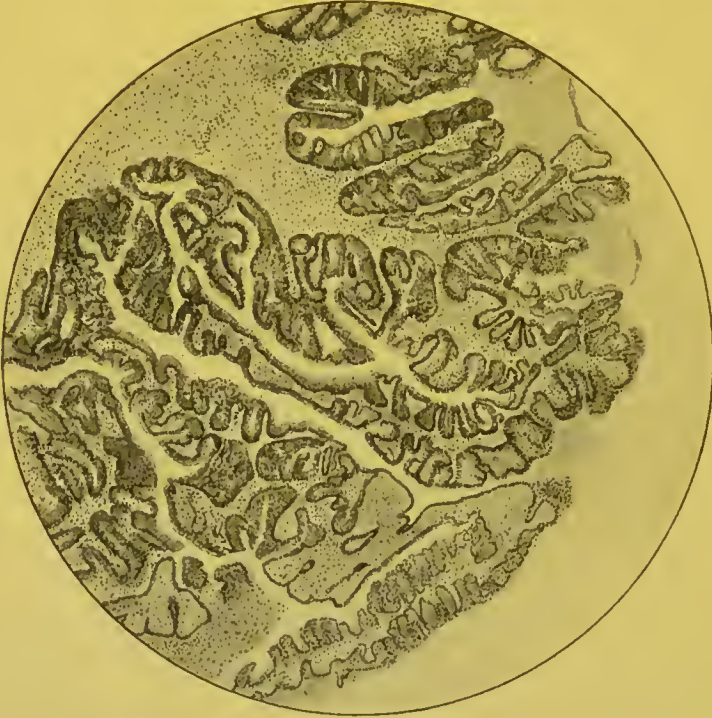


FIG. 98.—Papilloma of the common bile-duct. There is some adherent mucus on the surface of the growth. There is myxomatous degeneration of the fibrous core of the papilloma. (From the case referred to in the text, p. 687.) $\times 40$.

lesion in man is a pathological curiosity. A case of cystic tumours of the bile-ducts in man due to the irritation of these coccidia has been recorded by Podwyssozki.²

Papillomas or adenomas of the intrahepatic ducts may be multiple and give rise to no symptoms. On the other hand, there may be a single tumour, and in either case they may become cystic (*vide* p. 458).

The simple papillomas occasionally seen around the biliary papilla in the duodenum are growths of the intestinal surface of the papilla and not of the bile-duct. Papilloma may, however, arise in the cavity of the diverticulum of Vater. McPhedran³ described a case which, like most

¹ Eve. *Trans. Clin. Soc., Lond.*, 1906 xxxix, 144.

² Podwyssozki. *Centralbl. f. Bakt. u. Parasit.*, 1889, vi, 41.

³ McPhedran, A. *Sajous' Annual*, 1899, iv, 422.

A cystic Adenoma derived from, but not in communication with, the large extrahepatic ducts which it compressed was reported by Greg

Greg, D.M. Edin. med. Journ., 1921, N.S., XXVII, 145.

1912

Emm. R. Richardson
60. no gold stn
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of the cases of papillomatous growths around the duodenal orifice of the biliary papilla, gave rise to suppurative cholangitis.

A fibroma the size of a bean obstructing the lumen of the bile-duct has been described.¹

Volmer² reported an *adenomyofibroma* of the wall of the common bile-duct close to the ampulla.

Hydatid Cysts.—Devic and Gallavardin³ quote 3 cases in which hydatid cysts arose in the walls of the bile-ducts (Cadet de Gassicourt, Ignatieff, Macready).

Xanthoma, xanthelasma, or vitiligoidea has been found on the mucosa of the bile-duct in a few cases of chronic jaundice. It is the result of jaundice and not the cause. Fletcher⁴ described it in the bile-duct in a case of jaundice of ten years' duration due to calculous obstruction. In 2 cases mentioned by Fagge⁵ the lining of the bile-ducts was covered with the flat form of xanthoma.

MALIGNANT TUMOURS OF THE LARGER (EXTRA-HEPATIC) BILE-DUCTS

UNDER this heading primary malignant tumours of the extrahepatic bile-ducts will be dealt with. Carcinoma of the small intrahepatic bile-ducts is, for all practical purposes, primary carcinoma of the liver. Secondary growths are very rare in the bile-ducts, though in multiple malignant growths of the peritoneum they may be invaded from without. Extensions of growth to the bile-ducts from the hilum of the liver, from carcinomatous glands in the neighbourhood, from the lesser omentum, or from the pancreas are referred to elsewhere. Primary carcinoma of the ampulla or diverticulum of Vater is much the same as primary carcinoma of the lower end of the common bile-duct, but a separate description of this condition is given on page 702.

Incidence.—Malignant disease of the large or extrahepatic bile-ducts is probably not so rare as has been thought. The number of cases described has increased rapidly in recent years.

In 1889 Musser⁶ collected 18 cases; in 1897 Claisse⁷ tabulated 50; in 1901 Devic and Gallavardin,⁸ after excluding doubtful cases, analysed 55 examples, and I have notes of 90, about which there seems no doubt.

¹ Albers, quoted in von Ziemssen's *Cyclopaedia of Practical Medicine*, 1880, ix, 569.

² Volmer. *Arch. f. klin. Chir.*, Berl., 1908, lxxxvi, 160.

³ Devic et Gallavardin. *Rev. de méd.*, Paris, 1901, xxi, 571.

⁴ Fletcher. *Am. Journ. Med. Sc.*, Phila., 1905, cxxx, 949.

⁵ Fagge. *Principles and Practice of Medicine*, 1886, ii, 280.

⁶ Musser, J. H. *Boston Med. and Surg. Journ.*, 1889, cxxi, 581.

⁷ Claisse, P. *Gaz. des hôp. de Paris*, 1897, lxx, 1279.

⁸ Devic et Gallavardin. *Rev. de méd.*, Paris, 1901, xxi, 557.

The disease may be overlooked or more probably described as something else. Thus, some of the cases recorded as malignant tumours of the lesser omentum probably originated in the bile-ducts. Again, in some of the cases described as primary malignant disease arising in the portal fissure and involving the bile-ducts the growth may well have started in their walls. In other instances a slow-growing fibrous carcinoma of the bile-ducts has probably been described as a simple cicatricial stricture. In fact, to the naked eye there may be so close a resemblance that a microscopic examination is necessary to settle the question.

Etiology.—~~According to Zenker¹, primary carcinoma of the gall-bladder begins as an innocent papilloma which subsequently becomes transformed into a carcinoma. I have seen one case which~~ suggests that the same sequence might occur in the bile-duct.

A papilloma removed during a choledochotomy from the bile-duct of a woman was in immediate contact with a gall-stone which had been impacted for about two months. Some months later the patient returned with signs compatible with the view that the growth had recurred in the region of the operation wound, but did not remain under observation. I shewed the specimen to the Pathological Society² as an example of a papilloma due to irritation of a gall-stone; later on, after the patient's return, the question arose whether, supposing the recurrence to be carcinomatous, the growth had been malignant from the first, or whether the growth had subsequently invaded the duct-walls after the manner of a duct carcinoma in the breast. At the operation there was no infiltration of the bile-duct, so that if the recurrent growth was carcinomatous, it would appear that a transformation from a simple to a malignant adenoma had taken place.

It is conceivable that carcinoma may supervene on an ulcer of the bile-duct, as it does on an old gastric ulcer.

In a woman, aged fifty-seven, marked stenosis of the lower end of the bile-duct was thought to be due to cicatrization of an ulcer set up by a gall-stone. Microscopically there was carcinomatous invasion of the wall (Krokiewicz³). On the other hand, there is no proof that it was not a carcinoma from the first which had subsequently ulcerated.

In very rare cases (Necker,⁴ Taylor and Teacher⁵) primary carcinoma of the intrahepatic bile-ducts has been found in a liver occupied by independent secondary growths. Taylor and Teacher suggest that the irritation of these secondary growths played a part in the production of the primary growth.

Relation to Gall-stones.—Gall-stones are present in about a third of the cases of primary carcinoma of the bile-ducts; this contrasts with primary carcinoma of the gall-bladder in which gall-stones are met with in more than 70 per cent of the cases (*vide* p. 638).

¹ Zenker. *Deutsch. Arch. f. klin. Med.*, Leipz., 1889, xlv, 159.

² Rolleston. *Trans. Path. Soc.*, Lond., 1894, xlv, 83.

³ Krokiewicz. *Wien. klin. Wchnschr.*, 1898, xi, 320.

⁴ Necker. *Ztschr. f. Heilk.*, Wien u. Leipz., 1905, xxvi (*Abt. path. Anat.*), 351.

⁵ Taylor and Teacher. *Journ. Path. and Bacteriol.*, Cambridge, 1908, xii, 441.

It has been thought that
mentioned on p. 687

In 15 cases at the Mayo
Clinic Calculi were present
in biliary (Renshaw)

In Donati's 117. Collected cases, the common duct
was affected in 48, the function of cystic, common
and hepatic in 37, and the hepatic ducts in 32.

1914, Pm 137. F. 50
Lithiasis cystica v. common
Calculi in G.B.
1917. Pm. 411. F. 60
no calculi

no of "mature"
at "concretions"
F. 27 no calculi
M = 45 no —
M = 65 no —

Renshaw, K. Ann. Surg., 1922,

Donati. Quoted by Wilson, 1925, 1926
Rev. de Chir. Paris 1925, 1926, 316

4 9 In 67 of my cases in which a definite statement as to the presence or absence of gall-stones was made they were present in 23 and absent in 44. It is probable that in a high proportion of the cases in which no statement was made, gall-stones were absent. In 40 cases collected by Devic and Gallavardin¹ gall-stones were present in only nine instances—six times in the gall-bladder and on three occasions in the bile-ducts; in one case only was the growth found to surround the calculus. In Lapointe and Raymond's² 69 cases gall-stones were present in a fourth.

Sex.—Males are more often affected than females. In 83 cases, in which the sex is recorded, 50 males and 33 females were affected. This contrasts with carcinoma of the gall-bladder, in which females are attacked four times more frequently than males. 7/16

9 *Age.*—Primary malignant disease of the bile-ducts usually occurs after fifty years of age. This was so in 58 of my 83 cases. In Musser's³ 18 cases the average age was 56.6 years, and in 83 of my cases 55.5 years; in my series the average age was practically the same in the two sexes (55.5 in males, 55.4 in females); the extremes were 81 years in a woman and 29 in a man. 5

Morbid Anatomy.—*Situation of the Growth.*—Carcinoma may arise in any part of the larger bile-ducts, but it is very rarely confined to either of the two hepatic ducts.

In 90 cases the situation of the growth was as follows :

Common bile-duct :	
Lower end	23
Middle part	11
Junction of common bile-duct, cystic, and common hepatic ducts	27 8
Common hepatic duct	19
Right or left hepatic ducts	3 4
In cystic duct	6
In cystic duct and in lower end of the common bile-duct	1

The group of cases in which the growth is limited to the common hepatic duct or its two branches, the right and left hepatic ducts, has been called juxta-hepatic (P. Claisse³).

4 Of this form, of which I have collected 22 examples, Ingebrans,⁴ in 1902, tabulated 16. When juxta-hepatic carcinoma attacks the lower end of the common hepatic duct, it readily spreads to and occludes the cystic duct, and so becomes carcinoma of the junction of the common, cystic, and hepatic ducts. Devic and Gallavardin⁵ adopt a slightly different classification and divide their 54 cases into two groups: (a) Those in which the growth was in the common duct, or supra-duodenal, 22 cases; and (b) juxta- or sub-hepatic, 32 cases; among this latter category are included 15 cases of growth at the junction of

¹ Devic et Gallavardin. *Rev. de méd.*, Paris, 1901, xxi, 575.

² Lapointe et Raymond. *Arch. gén. de chir.*, Paris, 1908, ii, 375.

³ Claisse, P. *Presse méd.*, Paris, 1897, iv, p. cxxxix.

⁴ Ingebrans. *Arch. gén. de méd.*, Paris, 1902, cxc, 268.

⁵ Devic et Gallavardin. *Rev. de méd.*, Paris, 1901, xxi, 661.

the common bile, common hepatic, and cystic ducts. Lapointe and Raymond collected 32 cases in which the growth was in the hepatic duct, and 37 in which it was at the junction with the cystic duct.

When the cystic duct alone is affected, the condition is, both anatomically and clinically, much the same as carcinoma of the neck of the gall-bladder, and is, therefore, more conveniently grouped with

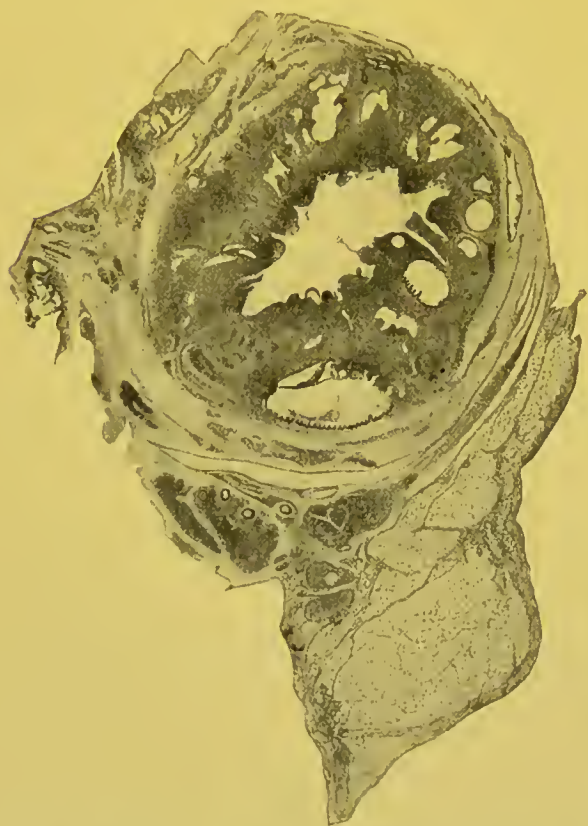


FIG. 99.—Section of common bile-duct with primary carcinoma. The growth projects into the lumen of the duct and narrows it. The muscular walls of the duct are infiltrated with growth. $\times 6$.

carcinoma of the gall-bladder. Few cases of carcinoma limited to the cystic duct have been recorded; this is probably because it either begins close to the gall-bladder and so spreads to it, or because it has extended into the junction of the common hepatic and common bile-duct by the time that the anatomical facts can be investigated.

Appearance of the Growth.—The growth is firm and white, and nearly always small—often not larger than a cherry. Large tumours are most exceptional; I have seen one as big as an orange. The growth may form a rather diffuse, infiltrating mass around the structures in the portal fissure, as in a case described by Planteau and Cochez,¹ and in 2 cases

which I have examined. In these instances it may be difficult to determine the origin of the growth, and the condition is sometimes described as primary carcinoma starting on the portal fissure. The tumour may be villous on its internal surface, but this appearance may be removed by ulceration; in this connexion it is interesting to refer again to the possibility that it may start as an innocent papilloma. Usually carcinoma is localised and infiltrates the walls of the duct, forming a firm annular stricture. Occasionally the growth spreads along the walls of the ducts, and transforms them into thick, rigid tubes. A considerable extent of the common bile-duct or even of the cystic or common hepatic

¹ Planteau et Cochez. *Rev. de méd.*, Paris, 1903, xxiii, 70.



ducts as well may thus be converted into carcinomatous tubes. In some instances the growth projects considerably into the lumen, and may thus produce obstruction rather than by an annular stricture. In one instance two apparently independent growths were found in the extra-hepatic bile-ducts. After death the stricture does not always appear to be absolutely impervious. It is probable that during life muscular spasm increases the obstruction. Haemorrhage occasionally takes place in connexion with the growth. It may be due to cholaemia, to erosion of a blood-vessel, or possibly to acute haemorrhagic pancreatitis.

Behaviour of the Growth.—Usually the growth does not infiltrate adjacent parts widely. It may grow into the substance of the pancreas, liver, or the portal vein. In a specimen (38·25) in the Hunterian Museum, Glasgow, a colloid carcinoma apparently of the common bile-duct invaded the abdominal wall. Carcinoma of the ducts may infiltrate the portal vein and cause thrombosis. As already mentioned, the growth may project into the lumen of the duct and thus obstruct it. It may extend along the walls of the ducts so as to involve widely the mucous membrane of the biliary tract, or it may spread along the lymphatics in the outer coats of the ducts and thus pass into the liver.

In one case in St. George's Hospital, a growth at the junction of the common bile, cystic, and common hepatic ducts spread up along the side of the hepatic ducts into the liver and produced a second stricture of the left hepatic duct inside the transverse fissure. In Planteau and Cochez's case, which was of much the same nature, a growth inside the left lobe of the liver was shewn to be an expansion of a continuous carcinomatous infiltration spreading along the ducts.

Naked-eye Diagnosis of Primary Carcinoma of the Bile-ducts.—Wherever it starts, the growth may spread along the ducts; thus a considerable extent of the common duct, together with the common hepatic duct and its branches, may be affected at the same time, or the gall-bladder, cystic duct, and the common bile-duct may be infiltrated in continuity. In such cases it may be impossible to determine its starting-point. As carcinoma of the lower end of the bile-duct may spread to the pancreas, and so present much the same naked-eye appearances as carcinoma of the head of the pancreas involving the common bile-duct, it is probable that some cases described as carcinoma of the head of the pancreas in reality started in the bile-duct. Microscopically carcinoma of the pancreas is spheroidal-celled, whereas that of the bile-duct is almost always columnar-celled; this provides a criterion for deciding the origin of the growth in any doubtful case. *ital*
1/3

As pointed out above, carcinoma of the bile-ducts at their exit from the liver merges into primary carcinoma of the liver; carcinoma of the cystic duct resembles malignant disease of the gall-bladder; some cases of carcinoma of the common bile-duct have probably been described as cancer of the gastro-hepatic omentum; and carcinoma of the lower end of the bile-duct may closely resemble disease of the head of the pancreas.

The disease is probably, therefore, less rare than is usually thought. On the other hand, malignant disease of the gall-bladder, or more rarely of the pancreas, may spread for a very considerable distance along the bile-ducts.

Thus in a woman aged fifty-six years, in St. George's Hospital, a spindle-celled sarcoma of the gall-bladder spread down along the cystic and common bile-ducts as far as the biliary papilla. In a case of Rose Bradford's¹ carcinoma extended from the gall-bladder along the cystic duct into the common bile-duct and hepatic duct, the growth terminating abruptly in all directions. When carcinoma arising in the head of the pancreas involves the common bile-duct and spreads along its walls beyond the confines of the pancreas, it may be difficult or impossible to be certain of the starting-point of the growth until a microscopic examination is made. Durante² described such a case.

Microscopical Appearances.—Duval³ described a unique case of primary melanoma of the lower end of the common bile-duct and ampulla of Vater; with this exception primary malignant tumours of the bile-ducts are carcinomas, and in the great majority of instances a columnar-celled growth derived from the surface epithelium.

In 43 cases which I have analysed, the tumour was a columnar-celled carcinoma in 37, spheroidal-celled in 5, and colloid in 1 (Leith⁴). In many cases the description is too vague to base any opinion on, the growth being spoken of as "scirrhus," "encephaloid," or merely as carcinoma.

It is possible that spheroidal-celled carcinoma of the bile-duct may be derived from mucous glands in its wall. Mucoid degeneration of the columnar cells leading to distension of the alveoli is not uncommon. In a certain number of the cases of columnar-celled carcinoma there is a transition to a spheroidal-celled character; this change is ~~commonly~~ ^{frequent} ~~seen~~ in carcinoma of other organs, such as the mamma and gall-bladder, and probably depends on increased rate of growth. It is often described as an atypical carcinoma. In rare cases mucoid or allied degenerative changes in the epithelial cells induce a swollen, flattened appearance, and as a result of the invagination of these cells an appearance closely resembling squamous-celled carcinoma is presented. As in the gall-bladder, metaplasia may give rise to a squamous-celled carcinoma (*vide* p. 632).

I am indebted to Dr. W. C. Bosanquet for the section from which Fig. 100 was made. In some parts of this section alveoli formed by flattened epithelial cells contained cholesterin crystals.

The supporting stroma of the tumour consists of well-formed fibrous tissue, shewing that it is slow-growing.

¹ Bradford, J. R. *Brit. Med. Journ.*, 1898, ii, 1555.

[.c/ ² Durante. *Bull. Soc. Anat. Paris*, 1893, lxxiv, 342.

³ Duval. *Journ. Exper. Med.*, N.Y., 1908, x, 465. This case was also recorded by Shepherd, *Ann. Surg.*, 1908, xlvii, 948.

⁴ Leith. *Trans. Med.-Chir. Soc. Edin.*, 1896, xv, 59.





Condition of the Bile-ducts.—Below the growth the calibre of the ducts is normal; it is possible that an impacted calculus might be situated below the growth and distend the distal portion of the duct. Above the growth the ducts are dilated, sometimes to such an extreme degree as to allow a finger or a thumb to be introduced. Dilated bile-ducts containing clear mucus, or in the early stages bile, may project on the surface of the liver. In rare instances infective cholangitis is present.

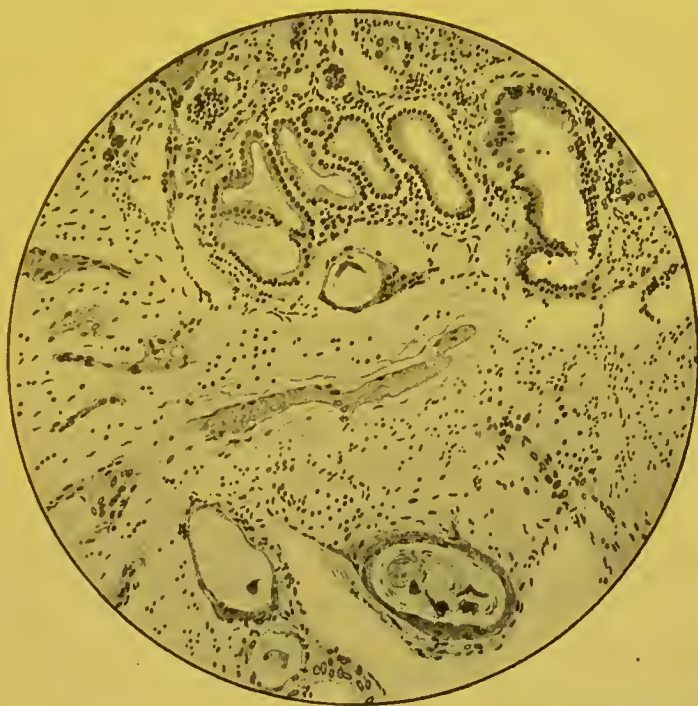


FIG. 100.—Microscopical appearances of carcinoma of the common bile-duct. The growth is columnar-celled in one part, but squamous-celled in others. The latter is an exceptional appearance. (From a specimen lent by Dr. W. C. Bosanquet.)

Condition of the Gall-bladder.—A tumour in the common bile-duct causes distension of the gall-bladder, unless, from former cholelithiasis, the gall-bladder is bound down by adhesions and retracted on itself.

In 18 cases in which the growth was in the common bile-duct the gall-bladder was distended in 17 (Devic and Gallavardin).

When the tumour is in the common hepatic duct, the gall-bladder is nearly always small; in exceptional instances it may be distended with mucus from concomitant obstruction of the cystic duct, or it may be occupied by gall-stones. When the tumour is at the junction of the cystic, common hepatic, and common bile-ducts, the gall-bladder is, as a rule, not enlarged, but from irregularities and variations in the degree of obstruction in the different ducts corresponding differences in the condition of the gall-bladder are met with. Lapointe and Raymond¹

¹ Lapointe et Raymond. *Arch. gén. de chir.*, Paris, 1908, ii, 375.

state that when growth is at the confluence, the gall-bladder is usually dilated.

Secondary growths are not very common, probably because the primary growth proves fatal from cholaemia before there is sufficient time for extensive metastases. They are most often found in the liver. In 57 cases the liver was affected in 13. Secondary growths may also arise in the adjacent lymphatic glands and in the peritoneum; in the latter situation they may produce ascites. Secondary growths very seldom occur when the primary tumour is in the common hepatic duct or in either of the two hepatic ducts. In 12 cases of this juxta-hepatic form of carcinoma of the bile-ducts analysed by Lecène and Pagniez¹ there was no instance of a secondary growth.

The *liver* shews dilatation of the bile-ducts, first with bile, but later with clear mucoid fluid. It may be either larger or smaller than natural, and is always of a very deep green colour. The liver cells atrophy, and there are areas of icteric necrosis.

According to Fütterer,² this icteric necrosis occurs in the central zone of the lobule, the intermediate and the peripheral zones remaining normal. This is explained on the theory that the distension of the interlobular bile-ducts compresses the interlobular channels and reverses the direction of the flow of bile. The bile then flows into the perivascular lymphatics around the central vein, and sets up necrosis of the neighbouring liver cells.

The liver cells contain bile-pigment, which may be regarded as being in the radicles of the bile capillaries. Around the necrosed areas small-celled infiltration and the formation of so-called new bile-ducts are sometimes seen. In the majority of cases there is no cirrhosis or fibrosis as the result of biliary obstruction. The atrophy of the liver cells allows the existing fibrous tissue to appear more prominent, and has led some writers to believe that biliary obstruction produces hepatic fibrosis. What to the naked eye looks like pericholangitic fibrosis may turn out to be new growth extending along the portal spaces. Weber and Michels,³ and Scagliosi,⁴ have insisted on the production of biliary cirrhosis in these cases. In cases in which the ducts have been infected there may be pericholangitic fibrosis. It is conceivable that hepatic cirrhosis may have existed prior to the development of malignant disease of the bile-ducts, or that some fibrosis around the ducts may have been induced by cholangitis due to gall-stones. Infection of the ducts, which is more likely to occur when the tumour is at the lower end of the common bile-duct, may give rise to suppurative cholangitis, empyema of the gall-bladder, and febrile disturbance.

Clinical Picture.—The *onset* is usually insidious, and generally the first thing noticed is jaundice, to which the patient's attention may be

¹ Lecène et Pagniez. *Arch. gén. de méd.*, Paris, 1901, clxxxvii, 176.

² Fütterer, G. *Chicago Med. Recorder*, 1897, xii, 325.

³ Weber and Michels. *Med.-Chir. Trans.*, Lond., 1905, lxxxviii, 261.

⁴ Scagliosi. *Riforma med.*, Palermo e Napoli, 1904, xx, 1210.

Poynton recorded an exceptional
case of Carcinoma of the
Common bile duct without
Jaundice.

Poynton. Brit. med. Journ., 1917, i, 483.

called by his friends. There may be an acute onset of gastro-intestinal symptoms, followed by jaundice and suggesting ordinary catarrhal jaundice; somewhat vague dyspeptic symptoms may exist for some little time before the appearance of jaundice. In a few cases the sudden onset of pain followed by jaundice imitates the impaction of a gall-stone in the common duct.

Symptoms.—Except when the tumour is in the cystic duct, jaundice is ~~always~~ present; it steadily progresses, and eventually becomes dark-green or black. There are gastro-intestinal symptoms, furred tongue, foul breath, dyspepsia, vomiting, and constipation, which may alternate with diarrhoea. The faeces are pale and to the naked eye quite devoid of pigment, but Cammidge¹ finds that hydrobilirubin can usually be detected; he concludes that the growth allows some bile to pass into the duodenum. There may be occult blood in the stools; in advanced jaundice there may be small gastro-intestinal haemorrhages from cholaemia. There may be distaste for fatty, or indeed for all food. The symptoms are largely those of jaundice combined with progressive loss of strength and flesh. Attacks of biliary colic, usually independent of cholelithiasis, are met with occasionally; this pseudo-gall-stone colic may be due to spasm of the ducts set up by the irritation of the growth, and is sometimes seen in malignant disease of the head of the pancreas. There may be dull pain in the right hypochondrium, but occasionally it is present on both sides. Pain is sometimes felt in the epigastrium, as in carcinoma of the head of the pancreas, and may then be due to invasion of the head of the pancreas by a growth starting in the lower end of the common bile-duct. Pain is not, as a rule, a marked symptom, but it may be so severe as to require the constant use of morphine.

Itching of the skin usually occurs when jaundice is well marked, but occasionally it precedes the appearance of icterus, and there may be little or no itching, even when the jaundice is very deep. The pulse is not slowed. The temperature is normal or subnormal in the absence of complications. I have seen it continuously raised for six weeks in a case in which inflammation was confined to a dilated bile-duct in the liver.

The gall-bladder becomes distended from backward pressure, and is palpable in about half the cases as a uniform smooth tumour. The smooth surface is important in distinguishing it from primary carcinoma of the gall-bladder. The gall-bladder is probably always enlarged, except when the growth involves the common hepatic or hepatic ducts, but it is not necessarily palpable during life. The condition of the liver varies considerably: sometimes it is enlarged and smooth from distension with bile; at other times, though large, it is concealed by tympanitic, or more rarely by ascitic, distension; but it may be normal in size. Secondary growths are very seldom felt during life; in fact, there is hardly time for extensive generalisation, as the disease kills comparatively rapidly by cholaemia. Secondary growths may cause ascites by pressing on the portal vein or by irritating the peritoneum. Ascites is not very

¹ Cammidge. *Proc. Roy. Soc. Med.*, Lond., 1910, iii (Med. Sect.), 163.

frequently prominent. It is, however, present in about half the cases examined after death (Devic and Gallavardin¹), and is often slight in amount and not of any clinical import.

The spleen is rarely palpable. In Devic and Gallavardin's 55 cases it was noted as palpable in 8.

The urine may be, but is not constantly, diminished in quantity, and is always deeply bile-stained. It often contains mucin. Albuminuria has been recorded, but, as a rule, there is no albumin or sugar. Casts may be present without albuminuria. Cammidge's test should give a negative result. This was so in two cases under my care in which the growth was in the common hepatic duct.

The progressive jaundice usually lasts about five or six months. The patient's condition is one of depression, the temperature being subnormal, unless some secondary infection occurs. Xanthopsia, in which everything the patient sees has a yellow tinge, is sometimes present. The usual duration of jaundice—five to six months—is not sufficiently long to allow of the development of xanthoma, which is usually associated with jaundice of considerable standing.² Pye-Smith,³ however, recorded xanthoma in primary carcinoma of the common duct. The symptoms of biliary toxæmia precede death, which may be from exhaustion, coma, or delirium. The biliary toxæmia is due to flooding of the blood by intestinal toxins normally stopped and either destroyed by the liver or excreted into the bile; this is due to a failure of the protective or detoxicating function of the liver. Haemorrhages into the skin and severe itching, when they occur, are due to this toxic condition of the blood. In rare instances death may be due to peritonitis set up by perforation of the gall-bladder. In the case recorded by May⁴ there were two gall-stones in the perforated gall-bladder; in Coats and Finlayson's⁵ case there was no history or sign of cholelithiasis.

Death may in very exceptional cases be due to haemorrhage in connexion with the growth. This occurred spontaneously in one case which I examined after death, and is a source of danger in cases in which any operative measures—such as cholecystenterostomy—are undertaken. In Huguenin's⁶ case the gall-bladder, which was full of blood, ruptured into peritoneal cavity and fatal haemorrhage resulted, 3½ pints of fluid blood being found in the abdomen.

Duration.—Usually death occurs from cholaemia within six months from the onset of jaundice. In one case under my observation jaundice had existed for thirteen months before an exploratory operation revealed carcinoma of the common hepatic duct.

Complications.—Besides haemorrhage around the growth and rupture

¹ Devic et Gallavardin. *Rev. de méd.*, Paris, 1901, xxi, 676.

² Vide a list of 23 cases of xanthelasma associated with jaundice tabulated in *Trans. Path. Soc.*, Lond., 1882, xxxiii, 381.

³ Pye-Smith. *Ibid.*, 1877, xxviii, 243.

⁴ May. *München. med. Wchnschr.*, 1892, xxxix, 590.

⁵ Coats and Finlayson. *Glasgow Med. Journ.*, 1890, xxxiv, 84.

⁶ Huguenin. *Virchows Arch.*, 1903, clxxiii, 552.

Carcinoma of the common
bile duct is not so likely
as pancreatic carcinoma
to exclude the pancreatic
ferments, & so examination
of the duodenal contents
may be of use

1

of the gall-bladder, suppurative cholangitis with or without multiple miliary abscesses has been known to occur. This is more likely to supervene when the growth is near the termination of the common bile-duct. As in cholelithiasis, infective endocarditis has been recorded, deep jaundice favouring infection. Thrombosis of the portal vein was found in Bourgeret and Cossy's¹ case.

Diagnosis.—The painless onset, the steadily progressive character of the obstructive jaundice, eventually becoming dark green, the age of the patient, namely, over fifty, and the absence of definite proof of any other cause are the factors which suggest malignant disease of the bile-ducts. But as it imitates obstructive jaundice due to other conditions, it will be advisable to consider the diagnosis between them seriatim.

Primary carcinoma of the head of the pancreas and primary malignant disease of the ducts are very much alike. In addition to jaundice, both these conditions may or may not shew dilatation of the gall-bladder during life, so this point does not help in the diagnosis. As regards pain, that of pancreatic carcinoma is epigastric, but from extension of the growth to the bile-ducts it may trespass into the hypogastric region. Enlargement of the liver has been thought to be more frequent in bile-duct carcinoma, and secondary growths in the liver are perhaps more often present in pancreatic cancer. In pancreatic disease the primary tumour is seldom, and in carcinoma of the bile-ducts it is almost never, palpable. In both cases the cachexia is rapid,—perhaps more so in cancer of the pancreas,—and death results from cholaemia. Some variation in the condition of the liver and gall-bladder, and in the site of pain, may occur in both. In short, a diagnosis between the two cannot be made on the foregoing grounds; and since pancreatic carcinoma is the commoner, it would, on the score of probabilities, be diagnosed whenever their common symptoms are presented. When carcinoma of the lower end of the bile-duct spreads into the pancreas, it may compress Wirsung's duct as well, and so lead to practically the same morbid condition as primary carcinoma of the head of the pancreas compressing the bile-duct. By his tests Cammidge² has found the following distinctive points: In carcinoma of the bile-ducts the saponified fat in the faeces is in excess of the unsaponified fat, whereas in carcinoma of the pancreas the saponified fat is less than or equal to the unsaponified fat. In carcinoma of the ducts the growth usually allows a little bile to enter the intestine, so that the faeces contain some stercobilin; in pancreatic carcinoma there is usually no stercobilin.

The differential diagnosis between primary carcinoma of the common bile-duct and of the ampulla of Vater is also extremely difficult (*vide* p. 706).

Gall-stones, impacted or lying in the common bile-duct, may be indicated by a history of biliary colic immediately preceding the onset of jaundice. But in a patient whose cystic and common bile-ducts are

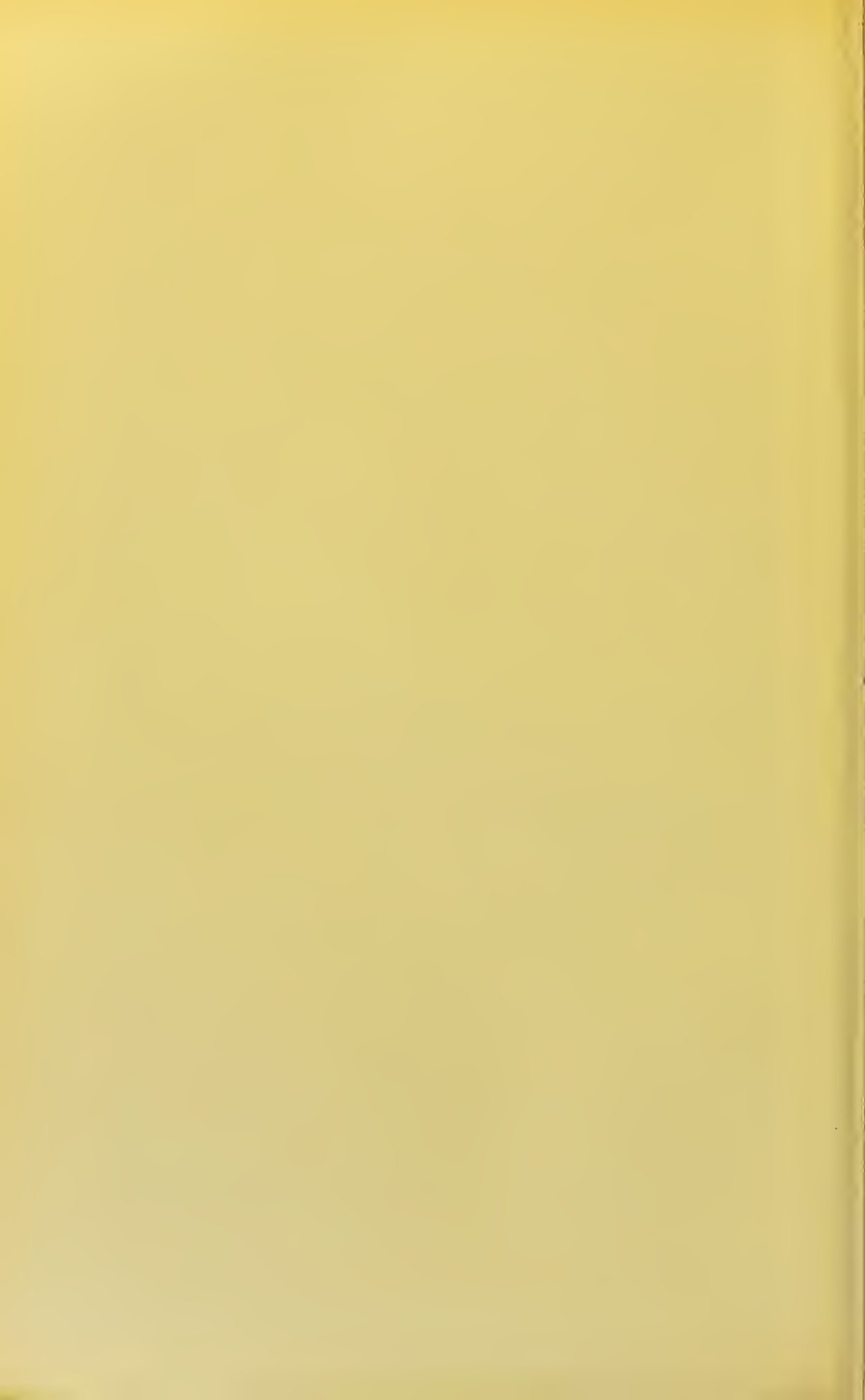
¹ Bourgeret et Cossy. *Bull. Soc. Nat. Paris*, 1873, xlviii, 347.

² Cammidge. *Proc. Roy. Soc. Med.*, Lond., 1910, iii (Med. Sect.), 163.

already dilated by the passage of gall-stones, impaction of a calculus may occur, especially near the duodenum, without any satisfactory history of its occurrence. In about a third of the cases of carcinoma of the bile-ducts calculi are found after death in the gall-bladder, and in a small proportion of these biliary colic has occurred in life. Conversely, pseudo-gall-stone colic may possibly occur in cases of malignant disease affecting the bile-ducts in the absence of any calculi. When biliary colic immediately precedes the onset of icterus, the diagnosis of cholelithiasis is more probable, but since gall-stones may enter the common duct without a characteristic history, it is desirable to consider any further points which bear on the diagnosis of gall-stone obstruction from that due to bile-duct carcinoma. The duration of calculous jaundice is very much longer than that of carcinoma of the bile-ducts, and death, when it occurs, is usually due to some complication, such as suppurative cholangitis, rather than to cholaemia. This difference in the course of the two affections is correlated with a difference in the nature of the obstruction in each case. In malignant disease the obstruction becomes more marked as time goes on, whereas with gall-stones the obstruction is complete at first, but subsequently, from the constant pressure exerted from within by the calculus on the wall of the bile-duct, from inflammation, and to some extent from extension of the dilatation of the ducts above the obstruction, the walls of the duct become somewhat separated from the calculus, and the obstruction becomes partial or so slight that eventually the jaundice may almost disappear. In gall-stone obstruction of the common duct periodic attacks of intermittent hepatic fever usually occur (*vide* p. 759) which are quite characteristic of this condition. The course and duration of the diseases, if uninterrupted by surgical treatment, are therefore sufficiently distinct to enable a differential diagnosis to be made, though this may not be possible in the earlier stages.

Courvoisier's law, namely, that in calculous obstruction of the common bile-duct the gall-bladder is not enlarged, whereas in obstruction of that duct by new growth the gall-bladder forms a palpable tumour, should always be borne in mind. But the gall-bladder need not be distended in all cases of carcinoma of the bile-ducts. Thus, in carcinoma of the common hepatic or of either of the hepatic ducts, the gall-bladder is not enlarged, and there may be difficulty in diagnosing the condition from impacted calculus in the common duct. The following points, then, would be in favour of cholelithiasis: The history of colic immediately before the onset of jaundice; intermittent hepatic fever; the chronic nature of the illness; the absence of enlargement of the gall-bladder, and the fact that, although of considerable duration, the jaundice is not very deep or progressive. Cammidge's tests are of use in the diagnosis: in gall-stone obstruction a positive pancreatic reaction is usually present, and there is urobilinuria pointing to cholangitis; in malignant disease of the ducts the pancreatic reaction is absent unless the growth irritates the pancreas.

So long as *primary malignant disease of the gall-bladder* is confined to



the gall-bladder and there is no pressure on the hepatic or common ducts, jaundice is absent, and there is no resemblance to primary carcinoma of the ducts. The jaundice is, therefore, no essential part of the disease, and is due either to extension of the primary growth or to pressure exerted by secondary growths on the bile-ducts. It occurs in the course of more than half the cases—according to Musser, in 69 per cent, which is also the proportion in which gall-stones were present in his 100 cases of carcinoma of the gall-bladder. When jaundice, due to obstruction of the duct, has supervened, the case is for all practical purposes one of malignant disease both of the gall-bladder and of the bile-ducts. Carcinoma of the gall-bladder may form a tumour, which is knobby or irregular, and is not so large as the smooth, dilated gall-bladder frequently met with in carcinoma of the bile-ducts or of the head of the pancreas. In addition to the history, the frequent association (70-95 per cent) of gall-stones with carcinoma of the gall-bladder should be kept in mind.

In *malignant disease of the liver*, whether primary or secondary, with jaundice, the history of the case and the facts that the liver is considerably enlarged and manifestly infiltrated with growth and that the jaundice is not so extreme, or, as a rule, of such long duration, will serve to differentiate it from primary carcinoma of the ducts.

From *hypertrophic biliary cirrhosis* there will seldom be any real difficulty in diagnosis. In some exceptional cases of bile-duct carcinoma the spleen is enlarged, but not to the same extent as in biliary cirrhosis. The latter disease occurs in younger persons, runs a chronic course, measured by years and not by months, and presents much greater enlargement of the liver and spleen.

Catarrhal jaundice is usually ushered in by vomiting and diarrhoea, while the onset of jaundice due to malignant stricture of the bile-duct is usually unobtrusive and unaccompanied by signs of gastro-intestinal catarrh. But the course of the two is so different—the one passing almost spontaneously away in a few weeks, the other getting progressively worse—that even if at first there be difficulty in determining which is the cause at work, little doubt remains after a few weeks have gone by.

There are a number of other causes which may sometimes give rise to chronic jaundice of varying degree, such as secondary malignant disease in the portal fissure, tumours or hydatid cysts in connexion with the liver, inflammatory adhesions, or even possibly gumma implicating the ducts, aneurysms of the hepatic artery or of the abdominal aorta—in short, most of the tumours and many of the morbid conditions to be met with in the abdominal cavity (*vide* p. 551). But the question of diagnosis between them and primary malignant disease of the ducts will seldom arise, inasmuch as there will generally be, either in the history or in the physical signs and symptoms, a clue to the nature of the disease.

Treatment.—The palliative and symptomatic treatment is that of

obstructive jaundice (*vide* p. 566). Pain may require morphine. For the treatment of pruritus see p. 567, but morphine should be given if other means are not successful. Calcium salts may be given both for pruritus and to prevent haemorrhages. Intestinal putrefaction may be combated by guaiacol, naphthalene tetrachloride, acetozone (1 in 2500), minute doses of calomel ($\frac{1}{40} - \frac{1}{20}$ gr.), and by preventing constipation by blue pill and salines. Cholaemia may be obviated temporarily by intravenous or better by subcutaneous transfusion if it is thought to be worth while.

Surgical interference has not been much in vogue, presumably because radical measures are very difficult. The palliative operation of putting the gall-bladder into communication with the small intestine—cholecyst-enterostomy—will, in favourable cases,—*i.e.* when the obstruction is limited to the common bile-duct,—prevent the bile being dammed up in the liver and absorbed by the lymphatics into the general circulation. In cases in which the obstruction is proximal to the junction of the cystic duct, a biliary fistula has been produced between a dilated duct in the liver and the outside of the abdomen (intrahepatic cholangiostomy) (Weber and Michels¹). Jaundice and cholaemia, with their attendant symptoms, may thus be obviated, and the patient's general condition greatly improved. As already mentioned, in complete biliary obstruction death is likely to occur from cholaemia, and if this is prevented, life may be greatly prolonged.

Curative Surgical Measures.—The resection of a growth from the bile-duct has been performed in a number of cases. Quénu² collected 9 cases—3 of the common bile-duct, 1 of the cystic duct, and 5 of the junction of the common bile, hepatic, and cystic ducts. Since then Littlewood³ successfully excised a growth of the cystic and common ducts.

A malignant growth of the cystic duct has been removed (Warren⁴), but this operation is more allied to excision of the gall-bladder and is not so difficult as resection of part of the hepatic or common bile-ducts.

MALIGNANT TUMOURS OF THE AMPULLA OF VATER

THE common bile-duct, before opening into the duodenum, joins with the main pancreatic duct; this common portion is called the ampulla or diverticulum of Vater. Normally the mucous membrane of the ampulla contains glands and is thrown into folds. It thus appears rougher than the inside of the common bile-duct, but it is not dilated except in definite pathological conditions, such as impaction of a gall-

¹ Weber and Michels. *Med.-Chir. Trans.*, Lond., 1905, lxxxviii, 247.

² Quénu. *Rev. de chir.*, Paris, 1909, xxxix, 245.

³ Littlewood. *Lancet*, Lond., 1910, i, 1341.

⁴ Warren. *Boston Med. and Surg. Journ.*, 1900, cxlii, 276.

In Nyström's case death from cholangitis followed
3 weeks after excision of a growth at the junction
of the cystic and common bile ducts.

NYSTRÖM, G. Acta Chir. Scandinav., Copenhagen, 1924, LVI, 85.

and Moll recorded a spindle-celled
sarcoma of the ampulla, in 1925

Outerbridge's collection of 110 Cases and
Clermont's 32 cases of ~~Carcinoma~~
of the ~~Ampulla~~ contained examples
in which the growth originated in
adjacent parts, such as the duodenal
surface of the Glands papilla

Moll, H.H. Journ. Path. and Bacteriol., Edin., 1925, xxviii, 528

CLERMONT. Rev. de gyn. et de chir. abdom., Par., 1913,
xx, 19

Souques et Aynard. Bull. et mém. Soc. méd. des hôp.
de Paris, 1907, 3^e série, xxix, 92

F 43

Upcott, H. Ann. Surg., 1912, Lvi, 710

M. 65. Gall. stone +

LEWIS, R.M. Surg. Gyn. & Obstet 1921, xxii, 543.

F. 45. no calculi

Dont type
F. 43 etc

stone. In 1908 Duval¹ described a melanoma of the lower end of the common bile-duct and of the ampulla of Vater. With these exceptions the primary malignant tumours of the ampulla of Vater are carcinomas. Carcinoma ~~may~~ start in the mucous membrane of the ampulla or ~~may spread to it from the lower end of the bile-duct or from the termination of the pancreatic duct.~~ ^{may}

Busson,² in 1890, collected 11 cases, and in 1896 Vincent Georges,³ a pupil of Hanot's, collected 9 more. ~~^ Hanot⁴ added another later in the same year. Of these 21 cases only about half a dozen are genuine examples of carcinoma of the ampulla of Vater, the others being carcinoma of the lower end of the bile-duct or of the duodenal surface of the biliary papilla.~~

I have collected ²²19 cases, ²⁰17 of them since the beginning of 1896, which appear to be undoubted examples of carcinoma arising in the mucous membrane lining the ampulla of Vater.

Hanot⁶ separated carcinoma of the ampulla of Vater from carcinoma of the lower end of the bile-duct, or, as it is called, juxta-ampullary carcinoma of the common bile-duct. He insisted that the growth is confined to the ampulla of Vater, and does not arise in the common bile-duct or in the duodenum. He spoke of the condition as *cancer du pylore pancréatico-biliaire*. The diagram overleaf shews his views. But the parts are so small that it may be difficult or even impossible to distinguish the form arising in the termination of the bile-duct (*vide* 1, in diagram) from that arising from the lining of the ampulla (*vide* 4, in diagram), away from the opening of the common bile-duct.

Primary carcinoma of the ampulla Vateri, or, as it might more conveniently be called, the choledcho-pancreatic duct, ~~must~~^{should} be distinguished from primary carcinoma—(1) of the termination of the common bile-duct; (2) of the termination of Wirsung's duct. According to Letulle⁷ primary carcinoma derived from the mucous membrane or glands of Wirsung's duct is spheroidal and not columnar-celled. This lesion has been very seldom recognised; Carnot and Harvier⁸ described a case in a

¹ Duval. *Journ. Exper. Med.*, N.Y., 1908, x, 465; also described by Shepherd, *Ann. Surg.*, 1908, xlvii, 948.

² Busson. *Thèse de Paris*, 1890.

³ Vincent Georges. *Thèse de Paris*, 1896, No. 404.

¹ Hanot, *Arch. gen. de méd.*, Paris, 1896, clxxviii, 547. Previous cases recorded by Hanot are given in Vincent-Georges' thesis.

⁵ Durand-Fardell, *Presse méd.*, 1896, 285; Vincent Georges, *Thèse de Paris*, 1896, No. 404; Rendu, *Soc. méd. des hôp.*, 1896; Hanot, *Arch. gén. de méd.*, 1896, clxxviii, 547; Pilliet, *Bull. Soc. Anat. Paris*, 1889, lxiv, 509; Domiciu, *ibid.*, 1896, lxxi, 709; Maury, *Bull. et mém. Soc. méd. des hôp.*, 1902, p. 433; Cornil et Chevassu, *Bull. Soc. Anat. Paris*, 1903, p. 151; May, *München. med. Wehnschr.*, 1892, xxxix, 590; Scheuer, *Berlin. klin. Wehnschr.*, 1902, xxxix, 138; Halsted, *Johns Hopkins Hosp. Bull.*, Balt., 1900, xi, 1; Pratt and Fulton, *Boston Med. and Surg. Journ.*, 1900, cxlii, 599; de Havilland Hall, *Lancet*, 1902, i, 1102; Klotz, *Montreal Med. Journ.*, 1904, xxxiii, 477; Moore, F. C., *Journ. Path. and Bacteriol.*, 1904, x, 76; Riva-Rocci, *Gazz. med. ital.*, 1904; Rolleston, *Lancet*, Lond., 1901, i, 467; and two from St. George's Hospital.

⁶ Hanot. *Arch. gén. de méd.*, Paris, 1896, clxxviii, 547.

⁷ Letulle, *Presse méd.*, Paris, 1906, p. 256; also Letulle et Verliac, *Bull. et mém. Soc. méd. d. hôp. de Paris*, 1905, xxii, 1063.

⁸ Carnot et Harvier. *Bull. et mém. Soc. méd. d. hôp. de Paris*, 1906, xxiii, 296.

woman aged sixty-six which was a transitional-celled carcinoma; Luzzatto¹ also recorded a case; and (3) of the mucous membrane covering the duodenal surface of the biliary papilla, or arising in Brunner's glands at this spot (Klotz²). This form of duodenal carcinoma is very commonly confused with primary carcinoma of the ampulla. It is not very rare, and there are specimens of it in the museums of St. Bartholomew's, Guy's, and St. Thomas's Hospitals. This lesion seems to be especially prone to lead to infective cholangitis and intrahepatic suppuration. The accompanying diagram illustrates these distinctions. Confusion may also occur between carcinoma of the head of the pancreas and primary carcinoma of the ampulla Vateri. Histologically they differ: carcinoma of the pan-

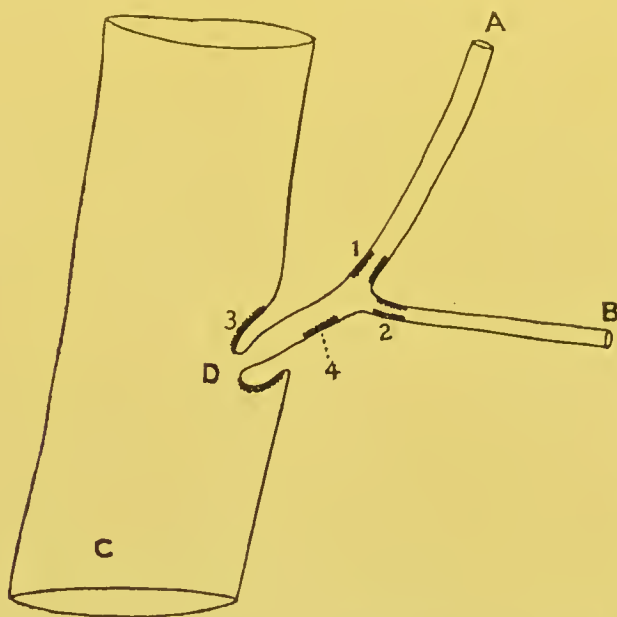


FIG. 101.—Diagram of the ampulla Vateri, shewing the various situations where carcinoma may arise in relation with it and in its neighbourhood.

A, Common bile-duct. B, Wirsung's duct. C, Duodenum. D, Biliary papilla. 1, Carcinoma of the termination of the common bile-duct. 2, Carcinoma of the termination of Wirsung's duct. 3, Carcinoma of the duodenal surface of the biliary papilla. 4, Carcinoma of the ampulla Vateri.

creas is spheroidal-celled, while carcinoma of the ampulla Vateri is columnar-celled.

Pic³ regarded carcinoma of the ampulla as an aberrant form of pancreatic carcinoma corresponding apparently with the excretory type (columnar-celled) of pancreatic carcinoma described by Bard and Pic.⁴

Morbid Anatomy.—The growth begins as a thickening of the mucous membrane of the ampulla and infiltrates its muscular walls. It may form a villous or polypoid tumour, and may then project through the orifice of the biliary papilla, which is dilated or ulcerated, into the duodenum. The growth is white, as a rule, but may be pinkish-white when projecting into the duodenum. It is comparatively small, and is rarely obviously ulcerated. It is probable, from the histological accounts, that some cases described as carcinoma of the Vater were simple

¹ Luzzatto. *Clin. med. ital.*, Milano, 1902, xli, 282.

² Klotz. *Montreal Med. Journ.*, 1904, xxxiii, 477.

³ Pic. *Rev. de méd.*, Paris, 1895, xv, 71.

⁴ Bard et Pic. *Ibid.*, 1888, viii, 394.

The parts are so ~~much~~ small that it may be difficult or impossible to distinguish where the growth arose, and recently cases of Carcinoma in the Vaterian region, but arising on the duodenal surface of the Bileamp papilla or at the termination of the common Bile duct or of Wirsung's duct have been described as Carcinoma of the ampulla of Vater. This appears to apply particularly to cases operated upon - For doubtful cases the term Carcinoma of the papilla of Vater is employed, of this Outerbridge has collected 112 cases.

OUTERBRIDGE. Ann. Surg. 1913, LVII, 402

In Moll's case of sarcoma
there was acute pancreatitis,
and this was ascribed to
regurgitation of the duodenal
contents, as the orifice of
the ampulla was patent.

papillomas. A growth in this situation, whether innocent or malignant, would rapidly give rise to jaundice and to cholaemia. Secondary growths are infrequent; Aynaud¹ estimates that metastases, nearly always in the liver, occur in 20 per cent of the cases. The patient probably often dies from cholaemia before there has been time for secondary growths to occur. If cholaemia is prevented by establishing a biliary fistula, as in the case given on p. 708, life may be sufficiently prolonged for secondary growths to develop.

Histologically it is, like primary carcinoma of the bile-ducts, practically always a columnar-celled carcinoma.

Pathological Results.—A growth in the ampulla of Vater may obstruct the orifice of Wirsung's duct and thus produce dilatation of the intrapancreatic ducts and chronic interstitial pancreatitis, as in the cases described on pages 707 and 708. As a result of this chronic interstitial pancreatitis diabetes might have been expected. This, however, does not occur. The explanation of this was given by Opie,² who shewed that obstruction of the duct is very seldom followed by the intimate fibrosis, which is accompanied by destruction of the islands of Langerhans, necessary to cause glycosuria.

If carcinoma of the ampulla of Vater involved the mucosa and walls of the orifice of the biliary papilla, it might, provided the growth did not obstruct the orifice of Wirsung's duct, convert the common bile-duct and Wirsung's duct into a continuous and closed channel. Bile might then enter the pancreatic duct and set up haemorrhagic pancreatitis. But in 11 cases of carcinoma of the ampulla of Vater collected by Dieulafoy³ there was no case of haemorrhagic pancreatitis. ~~The production of haemorrhagic pancreatitis by a small calculus impacted in the biliary papilla was described by Halsted and Opie⁴ (vide p. 750).~~

An ascending infection of the bile-ducts may induce suppurative cholangitis and multiple hepatic abscesses; this accident is more likely to occur than in primary carcinoma of the bile-ducts.

In a case recorded by Pratt and Fulton,⁵ the pus from multiple abscesses in the liver gave a pure culture of the *Bacillus aerogenes capsulatus*, but there was no gas-formation.

Etiology.—The male sex is much more often affected than the female sex, as is the case in primary malignant disease of the larger bile-ducts, whereas primary carcinoma of the gall-bladder is much commoner in 22 females. Of 19 cases 15 were males and 7 females.

It is a disease of advanced life. In 19 cases the average age was 55.2 years, being 56.4 years in the 15 males, and 52 years in the 7 22

¹ Aynaud. *Gaz. des hôp. de Paris*, 1907, LXXX, 807.

² Opie, E. L. *Journ. Exper. Med.*, N.Y., 1901, v, 397; *Diseases of the Pancreas*, 1903, p. 178.

³ Dieulafoy. *Presse méd.*, Paris, 1907, p. 657.

⁴ Halsted and Opie. *Johns-Hopkins Hosp. Bull.*, Balt., 1901, vii, 128.

⁵ Pratt and Fulton. *Boston Med. and Surg. Journ.*, 1900, cxlii, 599.

females. The extremes were 34 and 81 years. The average age of 16 cases collected by Aynaud was 62 years.

There is no relation between gall-stones and this form of malignant disease of the biliary system; in only 2 out of 19^{2/3} cases were calculi present. This is rather remarkable, since gall-stones are not infrequently found in the ampulla of Vater, and may remain there for very considerable periods, so that it might naturally have been assumed, on the analogy of the gall-bladder, that their irritation might give rise to carcinoma.



FIG. 102.—Columnar-celled carcinoma of the ampulla of Vater invading its muscular wall and the duodenum.

The symptoms, signs, and diagnosis of carcinoma of the ampulla are, in the main, the same as those of cancer of the common bile-duct (*vide* p. 697). The following points of difference bear on the diagnosis between the two conditions, which ~~must be regarded as a~~ very difficult problem:

(i) Jaundice is often intermittent, the faeces becoming normal in colour and the icteric tint of the skin diminishing or even passing off in the earlier stages when the obstruction is possibly valvular, or partly due to spasm of the duct set up by the irritation of the growth. In this connexion it may again be pointed out that confusion is apt to arise in recorded cases between carcinoma of the ampulla and of carcinoma of the duodenal surface of the papilla, in which jaundice is by no means constant. (ii) Intermittent hepatic fever and suppurative cholangitis are apt to occur. (iii) Diarrhoea is more often seen than in carcinoma

^ / namely jaundice, distension of the gall bladder, and emaciation from pancreatic insufficiency.



of the ducts, in which constipation is the rule. Attacks of diarrhoea may alternate with periods of obstinate constipation.

By his tests Cammidge is unable to differentiate between carcinoma of the ampulla of Vater and a stone in the common duct.¹ The clinical manifestations of the disease are illustrated by the following cases :

Carcinoma of the Ampulla of Vater ; Dilated Bile and Pancreatic Ducts ; Haemorrhage into the Pancreatic Duct.—A man aged sixty-six was admitted into St. George's Hospital under my care on July 22, 1900, with jaundice, pruritus, weakness, and wasting. He had never had any severe illness, and denied alcoholic excess and syphilis. Ten weeks before he had been quite well ; jaundice then appeared quite painlessly. A month later he began to waste, became weaker and drowsy ; two weeks later the skin began to itch. On admission he was deeply jaundiced ; the liver was enlarged and quite smooth ; the gall-bladder could be indistinctly felt ; the spleen could not be made out. The abdomen was somewhat distended, but there was no evidence of ascites. There was tenderness at a spot over the eleventh and twelfth ribs in the right hypochondrium. The urine contained albumin, bile-pigment, and bile acids, but no sugar. A tentative diagnosis of malignant disease of the head of the pancreas was made. On July 25 he had diarrhoea, on July 26 he vomited, had a rigor, and the temperature fell to 96° ; pulse 96, small. Respirations were 36 and the abdomen moved well. The liver seemed larger than on admission. He died eighteen hours after the onset of acute symptoms.

The necropsy shewed a small, hard tumour arising from the mucous membrane of the ampulla of Vater, and not visible from the duodenum. The growth blocked the pancreatic and common bile-ducts. The common bile-duct was as big as one's thumb and contained dark bile and mucus ; when opened and explored in a downward direction with the finger, it was found to end blindly, like a test-tube. The hepatic ducts and the ducts in the left lobe of the liver were widely dilated ; except the main hepatic duct, the bile-ducts in the right lobe were but little dilated. The cystic duct and gall-bladder were greatly dilated ; no calculi were found in the gall-bladder or in the bile-ducts. The liver (4 pounds) was smooth and of a deep green colour. Wirsung's duct was tortuous, dilated throughout its entire length, and near the head of the pancreas it formed a cyst into which recent haemorrhage had taken place. It is probable that the terminal acute symptoms depended on this haemorrhage. Towards the tail of the pancreas the duct contained dark fluid, probably altered blood of older date. The pancreas was attached to the posterior wall of the stomach by old adhesions. No calculi were found in the ducts of the pancreas. The pancreas itself was greatly fibrosed and hard. No secondary growths were found in any part of the body. The abdomen contained two pints of bile-stained fluid. The stomach and intestines shewed recent catarrh. Microscopically the growth was a columnar-celled carcinoma and invaded the muscular coat of the ampulla of Vater (*vide* Fig. 102). The pancreas shewed extensive fibrosis, some recent small-celled infiltration, dilatation of the ducts, which contained minute calculous masses, and widespread atrophy of the glandular tissue. The islands of Langerhans were intact.²

¹ Cammidge. *Proc. Roy. Soc. Med.*, Lond., 1910, iii (Med. Sect.), 205.

² This case was reported in the *Lancet*, Lond., 1901, i, 467.

Carcinoma of the Ampulla Vateri imitating Cholelithiasis.—A woman aged fifty-two was attacked six and a half months before death with colic, shivering, diarrhoea, vomiting, and distension of the abdomen. The pain lasted for two weeks and was succeeded by jaundice. She had several similar attacks resembling biliary colic, and when admitted to St. George's Hospital had lost three stone in weight. She was deeply jaundiced and complained of abdominal tenderness, itching of the skin, and weakness. Cholecystotomy was performed, but no calculi were found. At the operation there was ascites. Before death nodules of growth appeared in the skin around the fistula leading into the gall-bladder. At the necropsy, which I performed, a tumour projected from the gaping lips of the biliary papilla; it arose inside the ampulla of Vater and completely blocked the common bile-duct; the duct of Wirsung was obstructed and presented a cystic dilatation as large as a hen's egg near the tail of the pancreas, which was adherent to the fundus of the stomach. There were numerous secondary growths in the liver, which was small and deeply bile-stained. There was no cirrhosis microscopically, but numerous masses of inspissated bile were present in the minute bile-ducts. The growth was a columnar-celled carcinoma.

The treatment has usually been palliative and confined to relief of the symptoms, and on the same lines as in carcinoma of the bile-ducts.

Surgical Treatment.—~~Quénu¹ collected 9 cases treated by excision with 6 deaths, or 66·6. Oehler² has also reviewed the surgical treatment of carcinoma in this region.~~

Halsted³ successfully removed a primary carcinoma of the duodenal papilla and ampulla Vateri in a woman aged sixty. The common bile-duct and pancreatic ducts were engrafted into the duodenum; three months later the cystic duct was engrafted into the duodenum to relieve the biliary obstruction which had persisted. Death occurred within a year of the first operation from recurrent carcinoma in the head of the pancreas and duodenum, which had obstructed the openings of the common and cystic ducts into the duodenum. In a somewhat similar case Mayo⁴ removed a carcinoma of the terminal part of the common bile-duct by the duodenal route; it recurred in eighteen months.

¹ Quénu. *Rev. de chir.*, Paris, 1909, xxxix, 245.

² Oehler. *Beitr. z. klin. Chir.*, 1910, lxi, 726.

³ Halsted. *Johns Hopkins Hosp. Bull.*, 1900, xi, 1.

⁴ Mayo. *Boston Med. and Surg. Journ.*, 1903, cxlviii, 545.

of 20 Cases, described as Carcinoma of the ampulla and operated upon, 10 died of shock, and only 3 lived for 2 years or more (Clermont).
Lewis reported a case in good health more than 8 years after operation.
Kausch recommends that the operation should be done at two sittings: (1)
Cholecystenterostomy is performed in order to remove the jaundice (2) three weeks later the growth is removed

Clermont. Rev. de gyn. et de chir. abdom., Par., 1913, XX, 60

KAUSCH. Beitr. z. Klin. Chir., Tübing. 1912

Gallstones are said to have been first ~~q~~ observed by GENTILE da Foligno of Padua (died 1348).

The subject of the formation of gallstones will be ^{first} considered under the heads of (1) Aseptic calculus formation (2) Inflammatory calculus formation. After this the disposing factors and the relation of various factors and disease to cholelithiasis will be discussed.

- (1) ~~Whereas~~ Aseptic calculus formation: ~~See also~~ ^{of ROSSING} The work of Aschoff and his pupils Baerman ^{and} McNEE ^{and others} has profoundly modified Naunyn's doctrine that all calculi are due to inflammation of the gall-bladder.

CHOLELITHIASIS¹

~~The formation of gall-stones, whether in the ducts or in the gall-bladder, may be considered under the following two heads—(i) Immediate or exciting causes. (ii) Disposing causes.~~

Immediate or Exciting Causes.—According to Naunyn² the immediate cause of the production of calculi is a mild inflammation of the mucous membrane lining the ducts and gall-bladder. Catarrhal inflammation of the bile-ducts leads to an albuminous exudation which, as is also shewn experimentally by the addition of egg-albumin to bile, precipitates bilirubin in chemical combination with calcium as bilirubin-calcium calculi. This is the form of calculus usually found in the bile-ducts, though under conditions such as impaction of a gall-stone in the common duct, the formation of additional calculeous material containing cholesterol, as well as bilirubin-calcium, takes place. Simple stagnation and inspissation of bile do not lead to the precipitation of bilirubin-calcium or to the formation of bilihumin, which is constantly found in these bilirubin-calcium calculi. Something more than inspissation—viz. catarrhal inflammation—is necessary for the formation of these calculi. In catarrhal inflammation of the gall-bladder there is an abnormal formation of cholesterol, or cholesterol, as it has more recently been called, by the mucous cells and glands in its walls. ~~Evidence of this can be seen microscopically in the presence of myelin-bodies inside the cells.~~ This excessive and pathological production of cholesterol is responsible for the formation of multiple cholesterol calculi. This differs from the older conception that cholelithiasis was due to a mere precipitation of the cholesterol normally present in bile, brought about by a change in the bile, such as concentration or alteration in its chemical properties or reaction.

It was formerly thought that cholesterol formed elsewhere, and especially in the central nervous system, was picked up from the blood and excreted into the gall-bladder. ~~This explanation was abandoned since its administration by the mouth or under the skin in animals does not increase the amount in the bile.~~ Recently, however, Hürthle has shewn that cholesteryl oleate is constantly present in the blood; and

¹ For historical accounts of this disease the reader is referred to Thudichum's *Treatise on Gall-stones*, 1863, Churchill, London, and to Hoppe-Seyler, "Diseases of the Liver," Nothnagel's *Encyclopedia of Practical Medicine*, American translation, 1903.

² Naunyn. *Cholelithiasis*, p. 20. Translated by A. E. Garrod, New Sydenham Soc., 1896.

there is reason to believe that it is excreted into the gall-bladder, and that the oleic radicle is split off and re-absorbed by the epithelium of the gall-bladder (Adami and Aschoff¹), cholesterin being left in the gall-bladder. Aschoff and Bacmeister² believe that single pure (as apart from laminated) cholesterin calculi may be formed without any inflammation of the bile passages, and thus differ from multiple calculi which depend on catarrhal inflammation. The presence of a pure cholesterin calculus may favour infection, and so give rise to multiple gall-stones. For a discussion of the difficult subject of the origin of biliary cholesterin the reader should refer to Adami's *Principles of Pathology* (1910, i. 950).

It will be noticed that the results of catarrh in the small bile-ducts and in the gall-bladder differ both in the mechanism and in the nature of the calculi produced. As the result of catarrh of the small intrahepatic ducts there is a precipitation of bilirubin-calcium, whereas catarrh of the gall-bladder leads, by a perverted metabolism of the mucous membrane, to a pathological formation of cholesterin analogous to that sometimes seen in hydroceles and ovarian cysts.

The catarrh of the ducts and gall-bladder may be spoken of as lithogenic. If the catarrh starts in the ducts, the small calculi of bilirubinate of calcium may possibly find their way into the gall-bladder, and there form the nucleus of cholesterin calculi produced as the result of an extension of the inflammation to the gall-bladder. As catarrhal inflammation plays such an important part in cholelithiasis, it will be necessary to consider what are the exciting and disposing causes of catarrhal cholecystitis and cholangitis. The exciting causes are infection with micro-organisms and possibly the action of poisons excreted into the ducts.

The Microbic Origin of Gall-stones.—Galippe³ in 1886 first suggested that the formation of calculi depended on bacterial activity. Experimentally it has been shewn that the production of cholecystitis by the typhoid bacillus and the colon bacillus is followed by cholelithiasis. Non-virulent streptococci and staphylococci may also give rise to calculous formation; virulent cultures, however, set up intense cholecystitis without cholelithiasis (Mignot⁴). From Italia's⁵ researches it appears that pure cultures of streptococci or staphylococci may lead to the formation of calculi which are composed only of lime salts; cholesterin may be found when there is an admixture with cultures of the *Bacillus coli*. Thus experimental work, like clinical observation, shews that cholelithiasis is due to a comparatively mild cholecystitis, or, expressed in other words, is produced by an attenuated infection; this may depend on the preservation of the cholesterin-producing epithelium in the slighter forms of cholecystitis, and its destruction in more acute inflammations of the gall-bladder. Exner and Heyrovsky⁶ find that typhoid and colon bacilli

¹ Adami and Aschoff. *Proc. Roy. Soc., Lond.*, 1906, Ser. B., lxxviii, 359.

² Aschoff und Bacmeister. *Die Cholelithiasis*, 1909.

f.c/ ³ Galippe. *Compt. rend. Soc. Biol.*, Paris, 1886, 8. s., iii, 116.

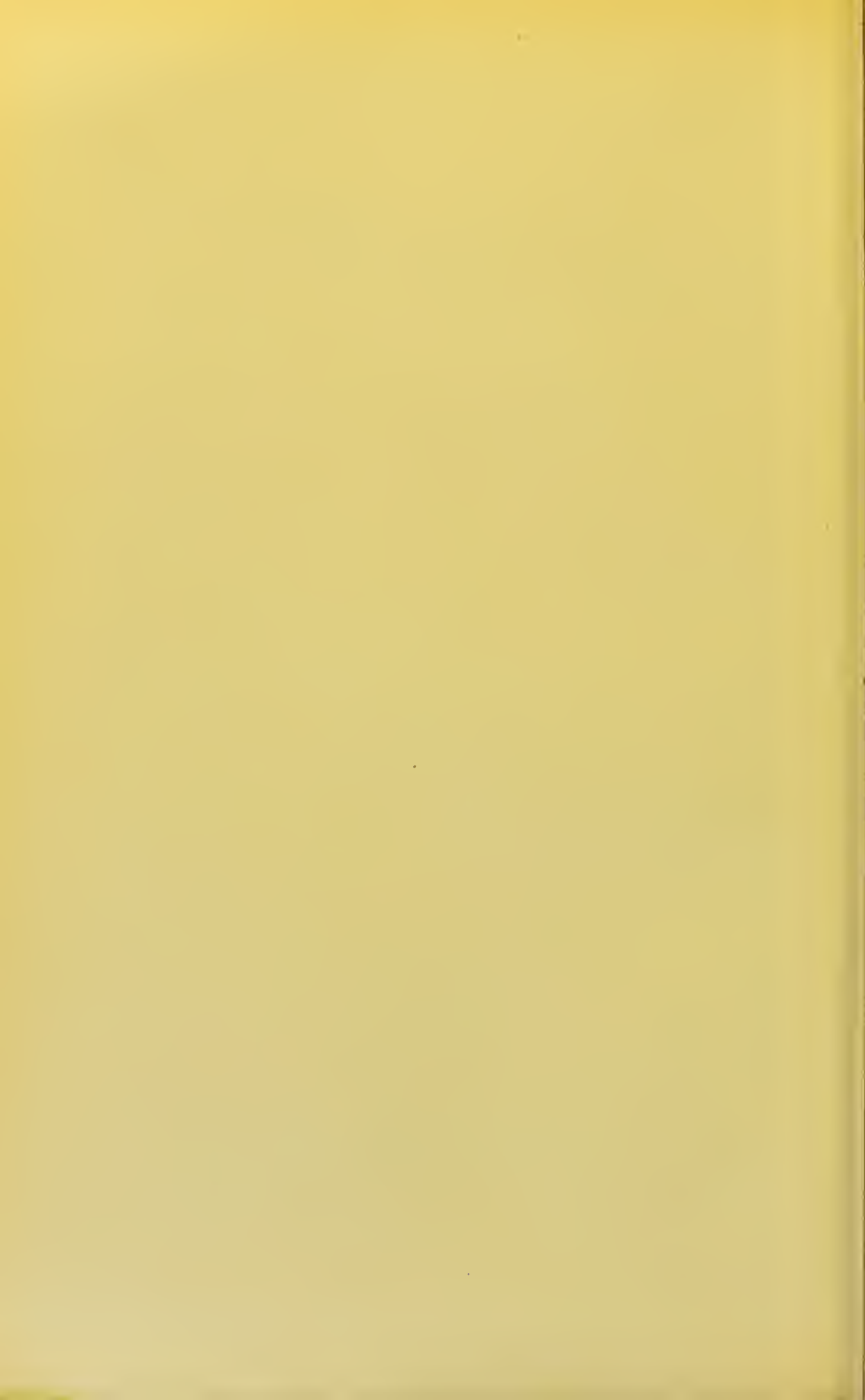
⁴ Mignot. *Arch. gén. de méd.*, Paris, 1898, clxxxii, 129.

⁵ Italia. *Riforma med.*, 1901, 830.

⁶ Exner und Heyrovsky. *Wien. klin. Wchnschr.*, 1908, xxi, 214.

From examination of 60 gallstone cases Reimann and Magoun found
that the cholesterol ^{content} of the blood was not ^{constantly} higher than in other
forms of inflammation in the right upper quadrant of the abdomen.
Campbell

Reimann, S.P. and Magoun, J.A.H. Surg. Gynec. and Obst., 1918, XXVI, 282.
Campbell,



destroy bile acids and so lead to a precipitation of cholesterin, but that streptococci do not have this action. The important micro-organisms in the production of cholelithiasis are: (1) The colon bacillus. (2) The typhoid bacillus.

(1) The main part in the microbial origin of biliary calculi is usually ascribed to bacilli belonging to the colon group. Mignot produced calculi in a guinea-pig as a result of the action of *Bacillus coli* on the gall-bladder in 1897. The colon bacillus has often been demonstrated inside biliary calculi (Welch,¹ Gilbert and Dominici,² Mignot); recent calculi especially shew the presence of bacilli; old calculi usually do not, or at best only the faintly staining shadows of micro-organisms. Droba³ found typhoid bacilli in a calculus seventeen years after the attack of enteric fever. Chauffard,⁴ who rather opposes the bacterial origin of cholelithiasis, has pointed out that the presence of micro-organisms in a calculus does not necessarily prove that they had any part in its formation, since they may invade a calculus from the outside.

It has been thought that the colon bacillus reaches the gall-bladder by an ascending infection of the common bile-duct from the duodenum. But bacteriological examination of the duodenum in health shews that during fasting the mucous membrane may be sterile, and that when micro-organisms are found they are, so to speak, accidental and derived from the ingesta (Cushing and Livingood⁵). Again, if the infection were ascending from the duodenum, the pancreas should be as often affected as the gall-bladder, since both their ducts open into the ampulla of Vater. Probably a condition of catarrhal inflammation of the duodenum would be necessary to render an ascending infection feasible. A factor of importance in the production of an ascending infection is more or less stagnation of the bile; otherwise the micro-organisms would be washed out of the ducts by the bile. On the other hand, it is highly probable that the *B. coli* reaches the liver by the portal vein and is excreted into the ducts.

(2) *Bacillus Typhosus*.—The causal relation between enteric fever and gall-stones was suggested by Bernheim⁶ in 1889, on clinical grounds, viz. the occurrence of symptoms in patients shortly after typhoid fever who had not previously had any signs of gall-stones. Calculi have often been found in the gall-bladder shortly after enteric fever in patients who had not previously exhibited any signs of cholelithiasis (Gilbert and Girode,⁷ Hanot,⁸ Hertz⁹). Dufourt¹⁰ found a history of enteric in 19 cases of cholelithiasis in which no symptoms of gall-stones had appeared

¹ Welch. *Med. News*, N.Y., 1891, lix, 669.

[.c.] ² Gilbert et Dominici. *Compt. rend. Soc. Biol.*, Paris, 1894, 10. s., i, 485.

³ Droba. *Wien. klin. Wochenschr.*, 1899, xii, 1141.

⁴ Chauffard. *Rev. de méd.*, Paris, 1897, xvii, 81.

⁵ Cushing and Livingood. *Johns Hopkins Hosp. Rep.*, Balt., 1898, ix, 543.

[.c.] ⁶ Bernheim. Art. "Ictère," *Dict. encycl. d. sc. méd.*, Paris, 1889.

⁷ Gilbert et Girode. *Compt. rend. Soc. Biol.*, 1893, 9. s., v, 958.

⁸ Hanot. *Bull. méd.*, Paris, 1896.

⁹ Hertz. *Proc. Roy. Soc. Med.*, Lond., 1910, iii (Clin. Sect.), 169.

¹⁰ Dufourt. *Rev. de méd.*, Paris, 1893, xiii, 274.

previous to the fever. In 12 of these cases symptoms of gall-stones appeared within six months of the attack of enteric fever. ~~In 42 cases of gall-stones 13 had had enteric fever and had not had any signs of cholelithiasis before the fever (Curschmann¹). A~~

Typhoid and paratyphoid bacilli (~~Blumenthal² (Cecil³)~~) have been found in calculi. Kramer⁴ has grown cultures of *B. typhosus* and of *B. coli* in bile and found that a precipitation of material comparable to that of a calculus results; he therefore explains the formation of gall-stones as due to this process and analogous to the formation of a triple phosphate precipitate in urine. In typhoid fever the *Bacillus typhosus* is almost constantly present in the gall-bladder after death, and, as a rule, without any calculous formation. It is, therefore, probable that the production of calculi depends on cholecystitis and not on the presence of micro-organisms alone. Typhoidal cholecystitis is described elsewhere (*vide* p. 605). The agglutination of typhoid bacilli in the bile has been suggested as a nucleus or starting-point for the formation of calculi (Richardson⁵), but this is not supported by experiments outside the body; Cushing⁶ added typhoid bacilli to bile and then precipitated them by adding the serum of a typhoid patient, but failed to obtain any precipitation of material from the bile.

Gilbert and Dominici,⁷ in 1893, in experimental typhoidal cholecystitis in a rabbit, produced greenish concretions. This was confirmed by Gilbert and Fournier⁸ in 1897. The question whether typhoid bacilli reach the gall-bladder by means of the portal vein or directly up the common bile- and cystic ducts has been discussed on p. 606. Here it may be said that it is more probable that the bacilli are carried to the liver by the portal vein and then excreted into the bile-ducts, and so reach the gall-bladder, than that there is an ascending infection from the duodenum. A

~~Cholelithiasis due to other Micro-organisms.~~—Pearce⁹ described cholelithiasis in a man aged fifty-nine years which seemed to depend on leptotrichial infection. The threads of leptothrix were found in the calculi. Cholecystitis and gall-stones due to *Micrococcus melitensis* have been recorded (Bull and Gram¹⁰).

Question of the Toxic Origin of Gall-stones.—The theoretical production of cholecystitis by poisons, such as perchloride of mercury, ricin, and by bacterial toxins has been referred to on p. 608. It was there stated that Wakeman¹¹ and Claude's¹² experiments make it probable that cholecystitis

¹ Curschmann. *Die Unterleibstyphe*, S. 355, Wien, 1898.

² Blumenthal. *München. med. Wchnschr.*, 1904, li, 1641;

³ Cecil. *Arch. Int. Med.*, Chicago, 1910, v, 510.

⁴ Kramer. *Journ. Exper. Med.*, N.Y., 1907, ix, 319.

⁵ Richardson, M. W. *Journ. Boston Soc. Med. Sc.*, 1899, iii, 79.

⁶ Cushing, H. *Johns Hopkins Hosp. Bull.*, Balt., 1899, x, 163.

⁷ Gilbert et Dominici. *Compt. rend. Soc. Biol.*, Paris, 1893, 9. s., v, 1033.

⁸ Gilbert et Fournier. *Ibid.*, 1897, xlix, 936.

⁹ Pearce, R. M. *Univ. Penna. Med. Bull.*, Phila., 1902, xiv, 217.

¹⁰ Bull og Gram. *Norsk Mag. f. Lægevidensk.*, Christiania, 1911, lxxii, 1026.

¹¹ Wakeman. Quoted by Herter, *Med. News*, N.Y., 1903, lxxxiii, 530.

¹² Claude. *Bull. méd.*, Paris, 1896, x, 714.

out of 161 cases of cholelithiasis 25, or 19.3 had had enteric fever (Chauffard). In a series of 100 cases of gallstones submitted to operation there was a history of ^{enteric} typhoid fever in 5 (Blaxland). Among 888 cases of gall bladder disease at the Johns Hopkins Hospital 28 per cent had had enteric fever. (Blalock).

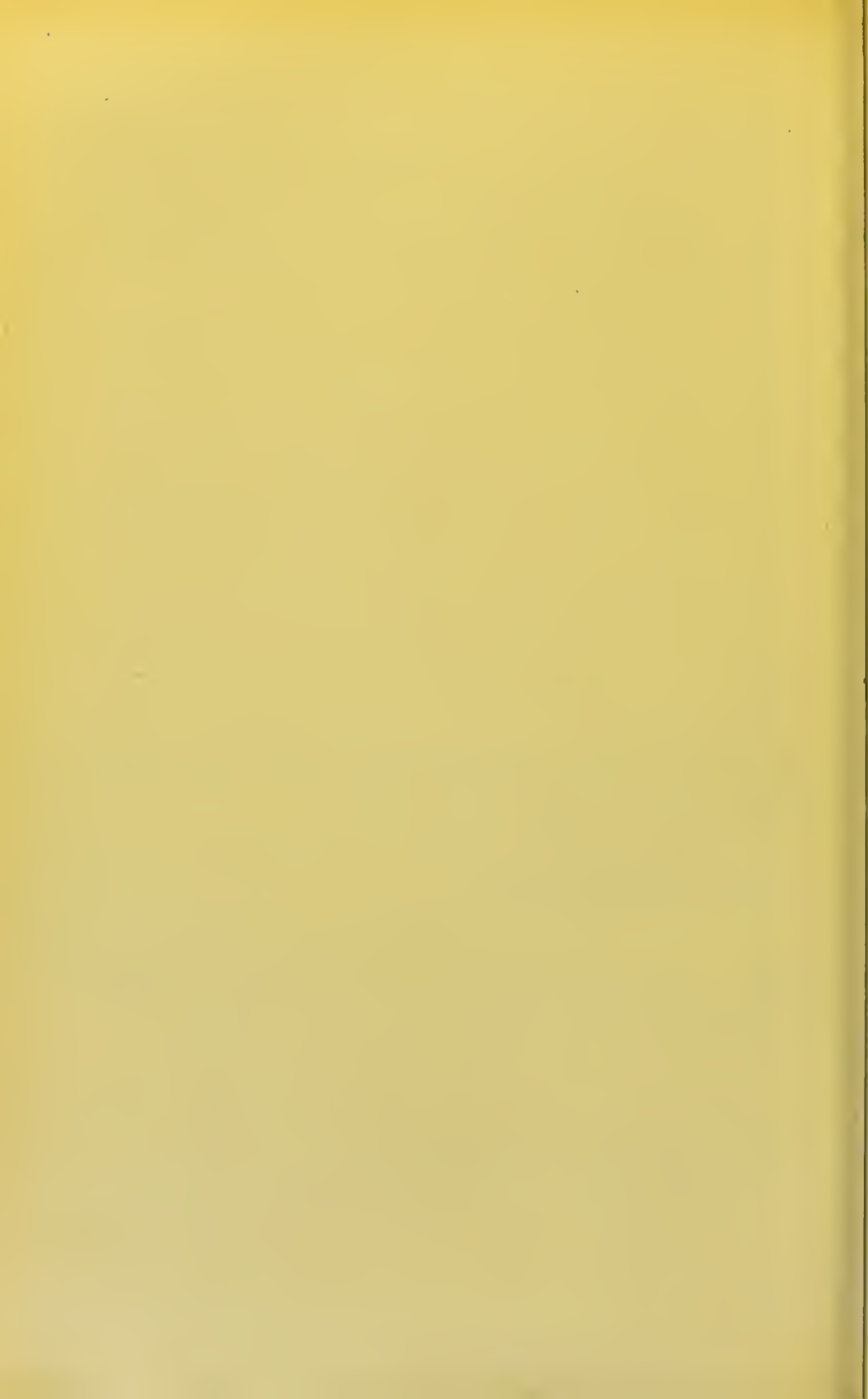
X In convalescence from enteric fever ~~the concentration of cholesterol in the blood is high and so the content in the bile and favours calculous formation~~ ~~cholesterol content of the blood is high and so the content in the bile and favours calculous formation~~ ~~But enteric fever has become rare in this country and gallstones have not; hence enteric fever takes a less prominent position now than formerly in the etiology of cholelithiasis.~~
~~Chauffard insists must be considered as an important factor in the production of gallstones.~~

B. enteritidis Gaertner (Dean)

Chauffard. Lecons sur la lithiase biliaire, Paris, 1914 p. 36
 Blaxland. Practitioner, 1914, xcii, 646.
 Forster und Kayser. Ibid., 1905, Lii, 147?;

Blalock. Bull. Johns Hopkins Hosp. Balt., 1924, xxxv, 291

DEAN, G. Journ. Hyg., Cambridge, 1911, xi, 259



may be produced by toxins. But though it might reasonably be expected (Gilbert¹), I am not aware that a toxic lithogenic catarrh of the gall-bladder has been produced experimentally. It may be concluded that although the production of gall-stones from catarrhal inflammation of the gall-bladder set up by poisons, without microbie intervention, is logically possible, it has not been shewn to occur in man.

Disposing Causes.—*Factors which favour the Production of Catarrh of the Gall-bladder and Bile-ducts, and so dispose to Cholelithiasis.*—1. *Stagnation of bile* in the gall-bladder renders infection more easy, since any micro-organisms which get into the bile are not removed. Further, in the absence of stagnation, micro-organisms present in the gall-bladder need not set up cholecystitis; this has been shewn experimentally by Ehret and Stolz,² and is supported by the constant presence of typhoid bacilli in the gall-bladder, often without any evidence of cholecystitis, in fatal cases of typhoid fever.

Sedentary habits, want of exercise, obesity, and diseases which necessitate a quiet life dispose to cholelithiasis. Want of exercise carries with it feeble contractions of the abdominal muscles, and as a result bile is not expelled so frequently or efficiently from the gall-bladder. This explains why gall-stones are rare in outdoor labourers and common in women. The influence of a sedentary life is shewn by the occurrence of biliary calculi in pet dogs and by their absence in wild animals. Sitting upright and leaning forwards over a desk keep the fundus of the gall-bladder in a dependent position and prevent, or at any rate inhibit, its proper evacuation. It has, therefore, been considered a disease of literary men, and has also been noticed in prisoners in gaol. The recumbent posture in an easy chair, however, favours the flow of bile out of the gall-bladder.

Tight lacing frequently leads to dilatation of the gall-bladder as the downward displacement of the duodenum strains and kinks the cystic duct, which even under normal conditions requires a spiral valve to keep it open (Keith³). Further, downward displacement of the right lobe of the liver makes the fundus of the gall-bladder more dependent than in health, and, since the cystic duct is more fixed at the transverse fissure of the liver, tends to produce kinking of the duct. A wandering liver has much the same effect. A floating kidney on the right side may, by traction on the peritoneum covering the common bile-duct in the lesser omentum, obstruct the outflow of bile from the gall-bladder. Any cause that interferes with diaphragmatic respiration, and therefore with the emptying of the gall-bladder, tends to produce stagnation of bile in the gall-bladder. Among the factors exerting this influence are tight lacing, abdominal distension from pregnancy, ascites, abdominal tumours, and cardiac and pulmonary disease.

2. *Foreign bodies* are exceptional in the gall-bladder. Aseptic foreign

¹ Gilbert. *Arch. gén. de méd.*, Paris, 1898, clxxxii.

² Ehret und Stolz. *Berlin. klin. Wchnschr.*, 1902, xxxix, 13.

³ Keith, A. *Lancet*, Lond., 1903, i, 689.

bodies do not give rise to cholelithiasis; this has been shewn experimentally by Mignot. If, however, cotton wool impregnated with colon bacilli is introduced into the gall-bladder, calculi are formed. Calculi have been found to contain pins or needles (Nauche,¹ Carless,² Eastman³), hydatid membrane, the ova of bilharzia (Gautrelet⁴), and round worms (Lobstein). Round worms may invade and infect the bile-ducts with micro-organisms from the duodenum, and in very rare instances may get into the gall-bladder. Five of Mertens'⁵ 48 cases of round worms in the bile-ducts were complicated by calculi. Hanot⁶ considered the worms the cause of the calculi, but Mertens thought the calculi dilated the bile-passages and facilitated the entrance of the worms.

Homans⁷ removed 97 calculi from the gall-bladder of a woman; twenty months later he again opened the gall-bladder for similar symptoms, and found 7 calculi crystallised on the sutures which lay free in the gall-bladder. In 3 patients operated on by Kehr⁸ recurrent colic was found to depend on calculous formation around sutures introduced at the first operation. Similar cases have been reported by Sinclair White,⁹ Malcolm,¹⁰ Drummond,¹¹ Floecker.¹² Haughton¹³ records a case of cholecystitis with gall-stones, in which a bristle and a piece of thread were found in the gall-bladder.

Foreign bodies favour stagnation and so inflammation, if microbes are present; microbes introduced alone may be removed with the bile, but if introduced together with a foreign body, they are enabled, as shewn by Mignot, to induce cholelithiasis.

Relation of Various Factors and Diseases to Cholelithiasis.—The influence of *diet*, ~~except in so far as it causes intestinal catarrh and so favours infection of the gall-bladder~~, is hard to estimate, and has attracted little interest since Naunyn's conception of a lithogenic cholecystitis became generally accepted. The belief that a saccharine and fatty diet favours cholelithiasis is probably true in virtue of its tendency to cause dyspepsia; but the explanation that a carbohydrate diet leads to a deficiency of bile salts, the solvents of cholesterin, is not of much value in view of the rarity of gall-stones in native Indians who subsist largely on rice. The view that a protein diet is not likely to cause cholelithiasis because it increases the quantity of bile salts may be

¹ Nauche; Lobstein. Quoted by Trousean, *Clin. Med.* iv, 230. Translated by New Sydenham Soc., 1871.

² Carless, A. *King's Coll. Hosp. Rep.*, 1897, iii, 101.

³ Eastman. *Journ. Am. Med. Assoc.*, Chicago, 1909, lii, 1660.

⁴ Gautrelet. *Union méd.*, 1885, Paris, 3. s., xl, 577.

⁵ Mertens. *Deutsche med. Wehnschr.*, 1898, xxiv, 358.

⁶ Hanot. *Arch. gén. de méd.*, Paris, 1896, clxxvii, 74.

⁷ Homans. *Ann. Surg.*, 1897, xxvi, 114 [Plate].

⁸ Kehr. *Gall-stone Disease*, p. 105. American transl., 1901.

⁹ Sinclair White. *Lancet*, Lond., 1907, ii, 443.

¹⁰ Malcolm. *Proc. Roy. Soc. Med.*, Lond. (Surg. Sect.), 1908, i, 96.

¹¹ Drummond. *Lancet*, Lond., 1908, i, 1206.

¹² Floecker. *Deutsche Ztschr. f. Chir.*, 1908, xciii, 310.

¹³ Haughton. *Med. Press and Circ.*, 1911, cxlii, 474.

~~Caplesco~~ Caplesco 18

Caplesco, C.P. Bull. Acad. Med., Paris, 1924, 3 ser.,
xcv, 869

met by the argument that it also increases the cholesterin in the bile (Goodman¹). Chauffard forbids foods, such as eggs, which increase the amount of cholesterin in the blood (*vide* p. 547).

Restriction in the amount of liquid taken by the mouth would tend to diminish the amount of bile and so to impair the freedom with which the ducts are flushed. Inasmuch as the amount of calcium in the bile is not affected by that taken by the mouth, it is very improbable that hard water induces cholelithiasis. Long intervals between meals lead to stagnation of bile in the gall-bladder and so favour infection. Kehr² suggests that the greater frequency of gall-stones among German women as compared with men may depend on their going to bed early and therefore fasting for a number of hours, while the late suppers taken by men empty the gall-bladder.

Excessive eating and alcoholism tend to induce gastro-enteritis, and hence cholecystitis and gall-stones are likely to occur in gross feeders, especially when of sedentary habits. Chronic venous engorgement of the portal system, whether from the backward pressure of heart disease, from cirrhosis of the liver or other causes, disposes to gastro-enteritis and so to cholelithiasis.

Anxiety and worry have often been regarded as a cause of gall-stones, and possibly act by inducing dyspepsia and constipation, and so reducing the resistance of the body as a whole, or possibly of the gall-bladder in particular, and so disposing to infection.

Indigestion.—While fully recognising that dyspepsia may be a manifestation of cholelithiasis, there is no doubt that persistent gastro-intestinal catarrh is an important cause of gall-stones. Abnormal bodies manufactured in the intestinal tract will tend to set up catarrh of the biliary tract, and infection of the gall-bladder by the portal vein or up the common duct may also be induced.

Constipation may increase intestinal catarrh and so dispose to infection of the gall-bladder; it may also, by leading to faecal accumulation in the hepatic flexure of the colon, interfere with the flow of bile through the cystic duct and thus produce stagnation in the gall-bladder. Further, intestinal catarrh may be partly due to vigorous purgatives taken to get the bowels open. Kraus³ found that 80 per cent of his patients with gall-stones at Carlsbad had constipation.

The relation between appendicitis and cholecystitis, and so with cholelithiasis, was mentioned on p. 604. It has been thought that cholecystitis may be due to infection from appendicitis, or from a gastric or duodenal ulcer (Ochsner,⁴ Sheldon,⁵ Moynihan⁶). Dieulafoy⁷ suggested that the appendicitis is secondary to the cholecystitis. There is some variation in the statistics dealing with the combination of cholecystitis and appendicitis.

¹ Goodman. *Beitr. z. chem. Physiol. u. Path.*, 1907, ix, 18, 91 (quoted by Adami).

² Kehr. *Gall-stone Disease*, p. 70. American transl., 1901.

³ Kraus. *On Gall-stones*, p. 20, 1896.

⁴ Ochsner. *Phila. Med. Journ.*, 1900, vi, 652.

⁵ Sheldon. *Journ. Am. Med. Assoc.*, Chicago, 1906, xlvii, 1458.

⁶ Moynihan. *Lancet*, Lond., 1912, i, 9. ⁷ Dieulafoy. *Presse méd.*, Paris, 1903, p. 445.

Becker¹ collected 34 cases in which the two conditions coexisted. In 46 cases operated upon for gall-stones, Sheldon found appendicitis in 39, or 85 per cent; whereas Kehr² in 720 laparotomies for diseases of the biliary tract found appendicitis in 18, or 2.5 per cent. Among 50 cases shewing gall-stones or cholecystitis, abstracted from the post-mortem records of St. George's Hospital, Mr. Frankau found that 2, or 4 per cent, shewed appendicitis; 6, or 12 per cent, gastric ulcer; and 2, or 4 per cent, duodenal ulcer.

Pregnancy.—Gall-stones often develop during or shortly after pregnancy. Naunyn³ estimated that 90 per cent of women with cholelithiasis had borne children, ~~Pregnancy in many women necessitates a very sedentary life, and is frequently accompanied by considerable constipation. It has been thought that the pregnant uterus impedes the descent of the diaphragm and so leads to failure in the expulsion of bile from the gall-bladder. Mosher,⁴ however, finds that pregnancy interferes less with the descent of the diaphragm than has been generally thought, and that respiratory movements tend to become equalised so that diaphragmatic respiration persists as late as the eighth month. It has been supposed that the enlarged uterus may compress the bile-ducts and so favour catarrh of the ducts and cholelithiasis (Körte, Heddaeus⁵).~~ Repeated pregnancies cause a relaxed condition of the muscular abdominal walls and so failure in the expulsion of the contents of the gall-bladder, and may be followed by visceroptosis. During pregnancy the blood contains an excess of cholesterol, ~~which is thought by Chauffard⁶ to favour cholelithiasis.~~

Glénard's disease or *visceroptosis* may dispose to cholelithiasis in several ways. In the general prolapse of the abdominal organs, kinking of or traction on the cystic duct may occur and obstruct the exit of bile. Nephroptosis on the right side may also lead to obstruction of the cystic duct, and so favour inflammation of the gall-bladder. Passive engorgement of the intestines may go on to catarrhal inflammation, and thus tend to lead to the same change in the gall-bladder. Keith⁷ states that gall-stones are almost invariably present in Glénard's disease.

Cardiac disease disposes to cholelithiasis in the first place by rendering life more sedentary and thus leading to stagnation of bile in the gall-bladder. Heart disease, in fact, makes the life of a male much the same as regards its sedentary character as that of women. In mitral disease with backward pressure gastric and duodenal catarrh are readily set up, and thus an ascending inflammation is favoured. The walls of the gall-bladder may be chronically engorged, and so more liable to become inflamed, ~~should infection be conveyed from the duodenum.~~ The influence of cardiac disease is shewn by statistics from the post-mortem room.

¹ Becker. *Deutsche Ztschr. f. Chir.*, 1903, lxi, 246.

² Kehr. *Die Therapie der Gallenwege*, 1902, iv, 456.

³ Naunyn. *On Cholelithiasis*, p. 40. Transl. New Sydenham Soc., 1896.

⁴ Mosher. *Johns Hopkins Hosp. Bull.*, Balt., 1901, xii, 253.

⁵ Heddaeus. *Beitr. z. klin. Chir.*, 1894, xii, 439.

⁶ Chauffard. *Rev. de méd.*, Paris, 1911, xxxi (B. bilé du Prof. Lépine), 177.

⁷ Keith, A. *Lancet*, Lond., 1903, i, 639.

Leano sur

1 and Schröder shows that gallstones are 10 times
commoner in fertile than in sterile women

the amount increasing from the normal 1.6 grams per litre to 6 ~~litres~~ and
derived from the corpora lutea and the adrenals (Chauffard)

W. J. N. E. Glasgow Med. Socy, 1914

~~J. B. K. E.~~

In 121 cases of diabetes at
Guy's Hospital gallstones were
found in 11 (Hale white)

Hale white. Lancet, Lond., 1914, i, 368

In 1347 successive necropsies at the Manchester Royal Infirmary gall-stones were found by Brockbank¹ in 101, or in 7.4 per cent. Of the 504 cases which shewed gross cardiac lesions biliary calculi were present in 55, or 10.9 per cent—males, 5.2 per cent; females, 22.6 per cent; while in 843 without cardiac disease calculi were met with in 46, or 5.4 per cent—males, 3.2; females, 10.2—so that a gross cardiac lesion seemed to double the incidence of cholelithiasis. This appeared to be almost equally true both for the males and females.

In 533 cases of cardiac disease collected from the post-mortem records of St. George's Hospital (F. A. Mills,² D. W. Bull³) the incidence of cholelithiasis in 350 males was 33, or 9.4 per cent, while in 183 females there were 31, or 17 per cent.

The statistics from St. George's Hospital also shewed that cardiac disease seems to affect the incidence of cholelithiasis by making it occur rather earlier in life than under ordinary conditions. In Brockbank's statistics mitral stenosis was much the most effective form of heart disease in inducing cholelithiasis; thus, in 87 cases gall-stones were present in 19, or 21.8 per cent, this being twice as high as in any other form of cardiac disease. In 533 cases of cardiac disease at St. George's Hospital the percentage of gall-stones, however, was a little higher in the aortic cases than in the cases of mitral disease.

In 72 cases of aortic aneurysm examined after death at St. George's Hospital (68 males, 4 females) there were no calculi; this shews that the causes of ~~arterial disease and~~ aneurysm, such as syphilis, strain, high ^{and} ~~tension~~, hard work, do not dispose to cholelithiasis. In fact, some of them, almost certainly hard work and exercise, tend to prevent it.

Pulmonary diseases, such as emphysema, which interfere with the movements of the diaphragm, or conditions such as chronic interstitial pneumonia, advanced emphysema, pneumoconiosis, which lead to failure of the right side of the heart and so to backward pressure, dispose to gall-stones.

Diabetes.—According to most statistics biliary calculi are rare in the bodies of patients dying with ordinary diabetes mellitus, and it may therefore be concluded that diabetes has no tendency to produce cholelithiasis.

In 220 cases of diabetes collected by Windle⁴ there was only one calculus, or 0.45 per cent. In 142 cases of diabetes (including 122 recorded by Seegen) there was only 1 in which a biliary calculus was mentioned.⁵ This scarcity Brockbank⁶ refers to the nitrogenous diet providing plenty of bile acids which keep the cholesterol in solution. In 50 cases of diabetes examined at St. George's Hospital calculi were found in 6. These figures are in antagonism to those

¹ Brockbank, E. M. *Edin. Med. Journ.*, 1898, iii, 51.

² Mills, F. A. Unpublished Thesis for M.B. Cantab., 1898.

³ Bull, D. W. *Ibid.*, 1908.

⁴ Windle. *Dublin Journ. Med. Sc.*, 1883, 3. s., lxxvi, 112.

⁵ Williamson. *Diabetes*, p. 119.

⁶ Brockbank. *On Cholelithiasis*, 1896.

just quoted, and are possibly explained by the fact, referred to below, that in 2 cases the diabetes was really secondary to chronic interstitial pancreatitis set up by gall-stones in the common bile-duct.

But although diabetes does not lead to the production of gall-stones, the converse does not hold good. Thus, if a calculus becomes lodged near the lower end of the common bile-duct, it may lead to infection and chronic interstitial pancreatitis, which may eventually become so extensive as to set up diabetes mellitus. I have seen at least 2 such cases, which are included among the 6 cases of diabetes at St. George's Hospital which shewed cholelithiasis. The occurrence of transient glycosuria during biliary colic is quite another question and is referred to on page 736.

To sum up, diabetes does not favour the production of gall-stones, but cholelithiasis may indirectly produce pancreatic diabetes.

Renal Disease.—In the arteriosclerotic and granular kidney the incidence of gall-stones is greatly increased, whereas no such influence is exerted by large white and contracted white kidneys. Inasmuch as *arteriosclerosis* and gall-stones both occur about the same period of life, it would be natural to find them often combined. In 115 cases of cholelithiasis Mosher¹ found that 50, or 43 per cent, had arteriosclerosis.

Among 357 cases of various forms of chronic nephritis collected from the post-mortem records of St. George's Hospital by A. W. Moore² there were 59, or 16·5 per cent, with gall-stones. Further analysis of these 357 cases yielded the following results:—In 261 cases of granular kidney, with an average age of 56 years, there were gall-stones in 56, or 21·4 per cent (average age, 59 years). In 49 cases of large white kidney, with an average age of 40, there were gall-stones in 2, or 4 per cent, and in 47 cases of small white kidney, with an average age of 34 years, gall-stones were present in 1, or 2 per cent. The greater incidence among the cases of granular kidney does not, as might at first sight appear, depend on the greater average age alone; for among the 261 cases of granular kidney there were 36 between the ages of 32 and 42 (thus including with a margin the average ages of the large white and small white kidneys), in 6 of which, or 16·7 per cent, there were gall-stones. Of these 36 cases, 11 were women, 4 of whom had gall-stones, or 36 per cent, and 25 men, 2 of whom, or 8 per cent, had gall-stones. Of the remaining 225 cases of granular kidney there were 138 men, 21 of whom, or 15·2 per cent, had calculi, and 87 women, 29 of whom, or 33·3 per cent, had calculi. The increased incidence of gall-stones in granular kidney therefore appears to be due to the high incidence of cholelithiasis in women with granular kidney. In the 261 cases of granular kidney the women were to the men as 3 to 5. The incidence of gall-stones in the 98 women was 33 per cent, and in 100 consecutive women over 40, dying in St. George's Hospital from all kinds of diseases, the incidence of gall-stones was 25 per cent. These figures are very small, but appear to shew that granular kidney increases the liability to cholelithiasis in women. It is possible that the increased formation of cholesterol in atheroma associated with granular kidney leads to a larger quantity of cholesteryl oleate in the blood and increased

¹ Mosher. *Johns Hopkins Hosp. Bull.*, Balt., 1901, xii, 253.

² Moore, A. W. Unpublished Thesis for M.B. Cantab., 1906.



excretion into the gall-bladder (cf. pp. 547, 709). This hypothesis is supported by the observation that in chronic nephritis the bile contains a high percentage of cholesterin—0·20 as compared with the normal 0·1 (H. Baldwin¹)—and that minute deposits of cholesterin are not uncommon in the gall-bladder (Herter²).

Myxoedema.—Many of the conditions favourable to the formation of gall-stones are present in this disease, such as the age (middle life), sex (female), and sedentary habits.³ According to Lorand⁴ cholelithiasis is favoured by ovarian inadequacy as well as by hypothyroidism.

Both in *portal cirrhosis* and in *biliary cirrhosis* it is rather surprising that biliary calculi are not commoner. In biliary cirrhosis there is catarrh of the small bile-ducts, and microscopic calculi or plugs of inspissated bile are often seen in the minute bile-ducts. In portal cirrhosis a secondary catarrh of the bile-ducts is not infrequent, and is certainly favoured by the condition of the liver.

In ²⁰⁰~~157~~ cases of cirrhosis examined after death at St. George's Hospital calculi were present in 23, or ¹³~~14·6~~ per cent, but in some of these 23 cases there were only small bilirubin-calcium calculi. In 233 cases of gall-stones examined after death in Calcutta there was cirrhosis in 18·2 per cent (Rogers⁵).

Minute bilirubin-calcium calculi are probably more frequent than is generally recognised in portal cirrhosis; they are small, and may easily escape observation.

Malignant Disease.—Musser⁶ suggested that the presence of malignant disease anywhere in the body favoured the formation of calculi in the gall-bladder. It would indeed be natural to expect that gall-stones would be found more often in the subjects of malignant disease than in ordinary routine post-mortem work; for carcinoma, which is the most frequent form of malignant disease, occurs, like gall-stones, most often in middle and later life. It is therefore remarkable that the following statistics do not shew a markedly increased incidence of gall-stones in patients dying with carcinoma.

In fifteen years 4616 patients were examined after death at St. George's Hospital. Of these, 268, or 5·8 per cent, had gall-stones. Among the 4616 cases 314 had carcinoma of some part of the body other than the gall-bladder; of these, 21, or 6·6 per cent, had gall-stones (199 males, 7 cases of cholelithiasis, or 3·5 per cent; 115 females, 14 calculi, or 12 per cent). This incidence of cholelithiasis was highest in primary carcinoma of the liver, uterus, and mamma.

Some statistics of malignant disease, such as Colwell's,⁷ shew a high incidence of cholelithiasis, but it must be borne in mind that both

¹ Baldwin, H. Quoted by Herter.

² Herter, C. A. *Med. News*, N.Y., 1903, lxxxiii, 531.

³ Vile Hertoghe. *Nouv. icon. de la Salpêtr.*, Paris, 1899, xii, 261.

⁴ Lorand. *Monthly Cycl. Pract. Med.*, Phila., 1906, N.S., ix, 252.

⁵ Rogers. *Ind. Med. Gaz.*, 1908, xliii, 408.

⁶ Musser, J. H. *Boston Med. and Surg. Journ.*, 1889, cxxi, 529.

⁷ Colwell. *Arch. Middlesex Hosp.*, 1905, v, 142.

malignant disease and gall-stones are commoner in women and in later life, and the influence of sex and age must not be regarded as the effect of malignant disease. Thus, in 44 cases of carcinoma of the mamma gall-stones were present in 16 per cent (Williams¹). Though this percentage would be high for ordinary routine work, it can easily be explained by the influence of sex and age, the subjects of mammary carcinoma being practically always women and usually over thirty-five years of age.

As is well known, gall-stones are present in from 70 to 95 per cent of cases of primary carcinoma of the gall-bladder, but there can be no doubt that the carcinoma is subsequent to and disposed to by the presence of calculi (*vide* p. 638).

In 13 cases in which secondary growths were present in the gall-bladder Siegert² found 2 cases with calculi, and in 19 similar cases, most of which I have examined myself, one only had a calculus. The local action of a secondary growth in the gall-bladder therefore does not favour cholelithiasis.

Uterine fibromyomas do not appear to be a factor in the causation of cholelithiasis.

Among 1224 women operated upon for uterine fibromyomas 7.5 per cent had gall-stones (Mayo³). Of 58 cases of gall-stones in women 13, or 22.4 per cent, had fibromyomas (Mosher).

Among the insane the percentage of gall-stones in routine post-mortem work is above the average; thus, at Claybury Asylum Candler⁴ found that among 2228 necropsies there were 315 with gall-stones or 14.13 per cent (females 17.85 per cent, males 9.9). Cholelithiasis is commoner in chronic melancholiacs than in acute maniacs; Keay,⁵ who quotes figures supporting this statement, believes that the stooping position of melancholiacs plays some part in the production of gall-stones.

Hereditary Influences.—The idea that cholelithiasis is an hereditary condition depending on a constitutional disposition is very old; Morgagni, indeed, insisted on the association of renal and biliary lithiasis, and has been followed by Bouchard, Chauffard,⁶ and others who believed that cholelithiasis was a manifestation of the "arthritic" diathesis, which included rheumatism, gout, and "uric acid." Lancereaux⁷ in 117 cases of much the same condition, which, however, he called "herpetism," found cholelithiasis in 47. No doubt sedentary habits, overeating, and dyspepsia favour the development of both gout and gall-stones, and the two conditions may occur in the same person; in 166 cases of gall-stones

¹ Williams, R. *Brit. Med. Journ.*, 1893, ii, 490.

² Siegert. *Virchows Arch.*, 1893, cxxxii, 353.

³ Mayo. *Journ. Am. Med. Assoc.*, Chicago, 1911, lvi, 1021.

⁴ Candler. *Proc. Roy. Soc. Med.*, 1911, iv (Path. Sect.), 87.

⁵ Keay. *Medical Treatment of Gall-stones*, p. 34, 1902.

⁶ Chauffard. *Ban. de méd.*, Paris, 1897, xvii, 81. *La lithiase biliaire*, p. 8, 1921.

⁷ Lancereaux. *Traité des maladies du foie et du pancréas*, p. 686, 1899.

Leçons 514

Among Chauffard's 161 cases of gallstones
34 per cent had a family history of the disease

An excess of cholesterol^{ol} in the blood
 has been found to accompany that
 of uric acid in the blood of the gouty
 (Chauffard, Brodin and Grigaut) but
 among 151 galeotons ^{among} ~~found~~ ^{Chauffard}
 found gout was rare. It appears that
 gout and urinary lithiasis favours a humoral
 state disposing to the acrific formation of
 galeotons, whereas the reverse does not hold
 good; urinary gravel is usually the earlier
 event in persons who have had both urinary
 and gall bladder calculi (Chauffard and
 Debray).

and among 1600 coroners' cases
 at Chicago 3.1 per cent. (Mitchell) } →

Comparing various European and American
 mortality records ^{Mitchell} found among 122,808
 cases 7022 with galeotons or 5.7 per cent.

Chauffard, Brodin et Grigaut. Compt. rend. Soc. Biol. Paris,
 1920, 672

Mitchell, L. J. Ann. Surg. 1918, LXVIII, 289.

Chauffard and Debray Presse med., Paris, 1925, XXXIII,
 129

collected by Sénac gout was present in 95. The view that any diathesis plays an important part has not met with so much support since it became clear that local inflammation of the gall-bladder is the immediate cause of gall-stones; Frerichs¹ and Naunyn,² in particular, have thrown the weight of their influence against the constitutional factor in cholelithiasis. Gilbert and Lereboullet³ have laid stress on a family tendency to catarrh of the biliary system (simple family cholaemia) which renders its subjects specially prone to various forms of jaundice, liver disorder, and lithogenic cholecystitis. It is probable that this diathesis, though not the sole or most essential factor, is of importance in the production of cholelithiasis, and it must not be forgotten that conditions of life and disposing factors, such as obesity, may be transmitted from one generation to another. Some statistics shew that gall-stones are hereditary in a large proportion of cases; this was so in 62 per cent of Kraus' Carlsbad patients. *Many of the latter found a hereditary history in 4 ranks, 51 per cent females.*

was recognized as
3/4 of cases
male
Occupation.—As already pointed out, sedentary occupations dispose to cholecystitis and gall-stones; it therefore occurs more frequently among the idle rich, hard-working literary men, clerks and devoted men of business, shoemakers, and in the poor in workhouses and asylums than in active persons whether well-to-do or tramps. Davy⁴ found that it was rare among soldiers, but possibly this is less true in these days of short service than in the first half of the last century. Among 472 patients at Carlsbad more than 50 per cent were professors, teachers, officials, or clergymen (Kraus⁵).

The incidence of gall-stones in routine post-mortem work varies somewhat in different countries; it is usually between 10 and 5 per cent.

In 10,866 cases obtained by combining the figures of Roth, Schloth, and Schröder gall-stones were present in 1029, or 9.4 per cent.⁶ This agrees with Kehr's⁷ estimate that one-tenth of the adult German population are the subjects of cholelithiasis. In America and England the percentage is lower. In 1655 American cases there were 115, or 6.9 per cent, with gall-stones (Mosher⁸). At the Middlesex Hospital Voelcker⁹ found gall-stones in 8.5 per cent, and Colwell,¹⁰ for a later period (1900–1904), in 5.4 per cent. Brockbank,¹¹ at Manchester, found 101 cases of gall-stones in 1347 necropsies, or 7.4 per cent; at St. George's Hospital there were ~~300~~ *300* in ~~4616~~ *4930* or ~~7.4~~ *6* per cent.

The percentage found in bodies examined after death is fairly represented by the statistics of a general hospital. The numbers would, of

¹ Frerichs. *Diseases of the Liver*, ii, 511, New Sydenham Soc., 1861.

² Naunyn. *Cholelithiasis*, p. 43, New Sydenham Soc., 1896.

³ Gilbert et Lereboullet. *Gaz. hebdomadaire de méd.*, Paris, 1902, vii, 889.

⁴ Davy, J. *Diseases of the Army*, p. 421, 1862.

⁵ Kraus. *On Gall-stones*, p. 19, 1896.

⁶ Naunyn. *Loc. cit.*, p. 144.

⁷ Kehr. *On Gall-stone Disease*, p. 99. American transl., 1901.

⁸ Mosher. *Johns Hopkins Hosp. Bull.*, Balt., 1901, xii, 253.

⁹ Voelcker, A. F. *Brit. Med. Journ.*, 1898, ii, 1555.

¹⁰ Colwell. *Arch. Middlesex Hosp.*, 1905, v, 145.

¹¹ Brockbank. *Edin. Med. Journ.*, 1898, ii, 51.

course, be extremely small in a children's hospital and disproportionately high in a workhouse infirmary.

Race and Geographical Distribution.—Gall-stones are rare in warm and tropical countries and are common in cold and damp cities, probably because these conditions tend to induce catarrh of the biliary tract.

Cholelithiasis is common in Germany, Austria, Sweden, Hungary, Russia, and is said to be infrequent in Holland, Finland, Denmark, and Italy. England probably comes about midway between these two groups. In America the percentage incidence is about the same as in England; ~~thus Mosher found it to be 7 per cent.~~¹ Among 4544 necropsies in India (93 per cent on natives, 7 per cent on Europeans) Rogers² found 233 or 5.4 per cent with gall-stones. The natives of Egypt are remarkably free from gall-stones (Day³). Gall-stones are rare in negroes, probably from their more active life and possibly from the good state of their teeth, in virtue of which they would not be exposed to infection of the alimentary canal from pyorrhoea alveolaris.

In America cholelithiasis is less common in coloured than in white patients; in 106 cases of gall-stones operated upon in Louisville only 1 was coloured.⁴ In routine post-mortem examination at the Johns Hopkins Hospital, Baltimore, however, the percentage incidence of gall-stones among blacks was 5.5 as against 7.9 among whites.

In England many cases come from the east coast, especially Lincolnshire. According to Ralfe⁵ the bleak country between Stafford and Wolverhampton and the damp valleys in Wales are responsible for many cases. Keay⁶ considers that it is commoner in Lancashire than in London.

Age.—The incidence of gall-stones increases as age advances. The majority of patients with cholelithiasis are over forty years of age, and it is rare before thirty.

G. Harley⁷ gave the following estimate: 75 per cent of cases occur in persons over forty; 20 per cent between thirty and forty; 4 per cent between twenty and thirty; 1 per cent under twenty. In Brockbank's⁸ 101 cases of cholelithiasis 79 were over and 22 under forty years of age. In ~~22~~ ³⁰⁰ cases in which gall-stones were found at St. George's Hospital ~~22~~ ¹⁰⁴, or 83 per cent, were forty or over. The largest number fell between the ages of fifty and sixty; of the ~~268~~ ³⁰⁰ cases, ~~99~~ ¹⁰⁴, or ~~37~~ ^{34.7} per cent, were in this decade.

The frequency of calculi in the gall-bladder in old age may possibly be due to senile atrophy of the muscular tissue in the walls of the gall-bladder and bile-duets (Chareot and Pitres⁹), which, by leading to stagna-

¹ Mosher. *Johns Hopkins Hosp. Bull.*, Balt., 1901, xii, 252.

² Rogers. *Ind. Med. Gaz.*, 1908, xliii, 408; *Glasgow Med. Journ.*, 1925, ciii, 110.

³ Day. *Lancet*, Lond., 1909, i, 258.

⁴ *International Textbook of Surgery*, Gould and Warren, 1900, ii, 741.

⁵ Ralfe. *Clin. Journ.*, Lond., 1895, vi, 281.

⁶ Keay. *Medical Treatment of Gall-stones*, p. 27, 1902.

⁷ Harley, G. *Diseases of the Liver*, p. 577, 1883.

⁸ Brockbank, E. M. *Edin. Med. Journ.*, 1898, iii, 51.

⁹ Chareot and Pitres. Quoted by Waring, *Diseases of the Liver*, p. 218, 1897.

In Japan the $\frac{1}{2}$ gallstones occur in about $\frac{1}{4}$ per cent of
all ^{new} autopsies and females are hardly more subject
to cholelithiasis than males as their work is active (Miyake)
and they do not wear stays.

and that in the Bengalis gallstones
are more frequent at every decade from
from the second, than

Miyake Arch. f. Klin. Chir.,

1913, C1,

In 1746 J. Gibson described gallstones in the
dilated common bile duct of a boy
aged 12 yrs whose gall bladder
contained 4 quarts of bile

Gibson, J. Medical Essays and Observations published
by a Society in Edinburgh, 1746, Vol II, p. 170

tion, favours infection and at the same interferes with the expulsion of calculi. Though calculi are very common in the bodies of old persons, especially in asylums and workhouses, symptoms of biliary colic are comparatively rare.

Cholelithiasis in Early Life.—Calculi are rare under twenty years of age. Cholelithiasis in early life may be divided into two classes :—

(i) Cases in which the process begins in intra-uterine life. A striking example of this category is Wendel's¹ case of a child eleven days old in whose gall-bladder there were 90 small cholesterin calculi. Thomson² collected 7 cases of jaundice in infants either stillborn or dying within the first month, in which gall-stones were present in the ducts. He suggests that gall-stone formation in infants and congenital obliteration of the ducts depend on the same inflammatory process. Still³ collected 10 cases, including Thomson's 7, in which small calculi were present in infants dying within a month of their birth.

(ii) Calculi in children. It is difficult to draw a hard-and-fast line between these two categories; and very possibly in cases in which the clinical manifestations are first noticed months or years after birth, the process began in intra-uterine life or depended, as Albu⁴ suggested, on some change in the ducts allied to congenital obliteration. Cholecystitis from typhoidal or colon infection may occur in early life; it is, indeed, rather surprising, in the face of the frequency of various forms of gastrointestinal infection in early life, that cholecystitis is so rare. It has been suggested that the application of a tight binder to a child's abdomen may, by inducing biliary stasis, dispose to the formation of calculi (Wendel). Small bilirubin-calcium calculi may be found in biliary cirrhosis, and are then due to inflammation spreading from the smallest bile-ducts—a descending cholangitis.

Still collected 23 cases under the age of fourteen years, 10 of which were in infants. Cases in children were previously described by Gourdin Servenière⁵ Mercat,⁶ and Trousseau.⁷ ^

Sex.—Gall-stones are more frequent in women than in men; the ratio has been variously estimated between five to one, and four to three. Schröder⁸ found gall-stones five times in females to once in males; Brockbank, four times in females to once in males; Harley,⁹ Kraus,¹⁰ and Colwell,¹¹ twice in females to once in males; Mosher,¹² three times in

¹ Wendel. *Med. Rec.*, N.Y., 1898, liv, 41.

² Thomson, J. *Edin. Hosp. Rep.*, 1898, v, 1.

³ Still, G. F. *Trans. Path. Soc.*, Lond., 1899, 1, 154.

⁴ Albu. *Deutsche med. Wchnschr.*, 1898, xxiv, 201.

⁵ Servenière. *Thèse de Paris*, 1889.

⁶ Mercat. *Ibid.*, 1884.

⁷ Trousseau. *Clinical Medicine*, vol. iv, p. 228. Transl. New Sydenham Soc., 1871.

⁸ Schröder. Quoted by Naunyn, *Cholelithiasis*, p. 40, 1896.

⁹ Harley. *Diseases of the Liver*, p. 575, 1883.

¹⁰ Kraus. *On Gall-stones*, English translation, p. 2, 1896.

¹¹ Colwell. *Arch. Middlesex Hosp.*, 1905, v, 142.

¹² Mosher. *Johns Hopkins Hosp. Bull.*, Balt., 1901, xii, 253.

females to twice in males. In 268 cases in which gall-stones were found after death at St. George's Hospital the number of women (153) was in excess of the males (115) in the ratio of 4 to 3.

The factors determining the greater incidence of gall-stones in women are: (i) A lax condition of the abdominal walls, which favours visceroptosis and so disposes to hepatoptosis. As a result, stagnation of bile in the gall-bladder, a condition facilitating infection, is brought about. (ii) Abdominal tumours, such as uterine myomas and ovarian cysts, and the pregnant uterus produce relaxation of the abdominal wall and interfere with diaphragmatic respiration. (iii) Tight lacing may act in several ways: by displacing the liver it may kink the common or cystic ducts and mechanically obstruct the outflow of bile from the gall-bladder. It also diminishes diaphragmatic breathing and increases costal respiration. The movements of the diaphragm are of importance in emptying the gall-bladder, and hence if they are diminished, stagnation of bile follows. (iv) The sedentary life led by most women. (v) Constipation is common in women and favours infection of the bile-ducts and gall-bladder. (vi) Pregnancy (*vide* p. 716). (vii) The frequency of pelvic infections may be of some importance by serving as a source of infection or by producing peritoneal adhesions which may interfere with the free exit of bile from the gall-bladder (Mosher¹).

The following classification of gall-stones, according to their chemical composition, is based on that given by Naunyn:—

I. *Solitary pure cholesterin calculi* are comparatively uncommon. They are white, yellow, or more rarely brown or greenish, and have a translucent appearance. The surface is nodular, crystalline, or smooth. There is a nucleus of pigment with radiating crystals of cholesterin around it. On section they are crystalline, but not stratified. They are formed in the gall-bladder when the cystic duct is blocked. They are single, and very slow in formation. According to Aschoff and Bacmeister² they are formed without any previous inflammation of the gall-bladder.

III. *Laminated cholesterin calculi* contain from 75 to 90 per cent of cholesterin, with calcium carbonate and traces of bilirubin and biliverdin in combination with calcium. ~~Externally they resemble pure cholesterin calculi, and are also single.~~ On section, there are alternating laminae—white and brown, yellow or green. The coloured layers contain bilirubin-calcium when brown, and biliverdin-calcium and calcium carbonate when green.

IV. *The Common Gall-stones (Mixed Cholesterin and Bilirubin-calcium)* ~~They vary in size and colour. There may be a single large barrel-shaped calculus filling the gall bladder, or they may be multiple, and are then usually faceted, are seldom larger than a cherry, and may be very small and numerous. They are usually yellow, but may be brown or white.~~

¹ Mosher. *Johns Hopkins Hosp. Bull.*, Balt., 1901, xii, 253.

² Aschoff und Bacmeister. *Die Cholelithiasis*, 1909.

Aschoff

II The combination calculus, composed of a pure cholesterol^{ol} stone modified by the results of cholecystitis, is usually single, but there may be other calculi in the gall bladder. Aschoff found that combination stones with or without other calculi constituted 20 per cent of all gallstones. They

form 60 per cent of all gallstones. They are always,

They are always built up concentrically and ~~never~~ have any radiate structure (MENEZ).



When fresh, they are greasy and soft, but when dried, they become hard externally. There may be a central cavity inside.

IV. *Pure Bilirubin-calcium Calculi*.—They vary from the size of a pea to a grain of sand. There are two types: one is solid, brown in colour, rough on the surface, and with a tendency to become welded together. The second type is harder, smooth, black, has a metallic lustre, and internally a spongy structure; ~~they contain 65 per cent of bilirubin-calcium~~ *like graphite*.

V. *Rarer Forms*.—(a) *Amorphous and incompletely crystalline cholesterin gravel*: these small calculi may look like pearls; the nucleus is of different composition—often of bilirubin-calcium. (b) *Calcium carbonate calculi* are very rare; these calculi give a shadow with *x*-rays, other gall-stones do not. (c) *Calculi containing foreign bodies*, such as fragments of worms, ligatures (*vide* p. 713). (d) *Conglomerate calculi*, which are composed of two or more small calculi united under a common sheath. (e) *Casts of bile-ducts* are very rare in man; bilirubin-calcium casts are found in cattle.

Mode of Formation of Calculi in the Gall-bladder.—There are two explanations of the formation of gall-stones in the gall-bladder: Naunyn's, that it is due to inflammation of the lining mucosa of the organ, and Aschoff and Bacmeister's view (*vide* p. 710) that solitary pure cholesterin calculi may form independently of inflammation. The latter observers admit that the presence of a pure cholesterin calculus favours infection and inflammation of the gall-bladder, and that as a result multiple calculi containing calcium may result. Naunyn's explanation is as follows: The cholesterin from which the calculi are, in the first instance, largely formed, is not derived from the bile itself, but from the disintegration of the cells lining the gall-bladder, and is the outcome of perverted metabolism induced by catarrh. Cholesterin is formed by other mucous surfaces, but calculus-formation does not result, since there is an absence of the necessary cementing substance. The cementing substance is bilirubin-calcium. Masses of cholesterin mixed with bilirubin-calcium form the earliest stage of a calculus. The further development may proceed in different ways: The mass may become surrounded with a firm crust of bilirubin-calcium, while the cholesterin and bilirubin-calcium crystallise out on the inner surface of the outer crust, thus leaving a central cavity. Or the firm outer layer may be produced by drying, starting in the outer layer of the mass of bilirubin-calcium and cholesterin, after which crystallisation takes place inside the shell with the production of a central cavity as before. So far the formation of an immature calculus has been traced; the further changes leading to the growth and formation of a stratified and more solid calculus are as follows:—

The growth of a calculus is chiefly the result of deposition, on its surface, of concentric layers of cholesterin and of bilirubin-calcium or biliverdin-calcium. The cholesterin forms white laminae, and is deposited, not as crystals, but as a pultaceous mass of myelin bodies supplied by the cells of the gall-bladder. In the formation of pure cholesterin calculi the gall-bladder contents must be free from any bile, as in cases of obstruction of the cystic duct. Bilirubin-calcium forms brown and bili-

verdigris green strata; their deposition occurs when the gall-bladder contains bile. The calculus becomes infiltrated from without by cholesterin, exactly in the same way as a calculus in the urinary bladder is invaded by phosphates and other salts. The secondary infiltration of a gall-stone with cholesterin may be derived from the epithelial walls of the gall-bladder, if in contact with it, or from the cholesterin in the bile. The cholesterin tracks along small fissures and canals into the interior of the calculus; it then forms crystals which increase in size. This process begins at the centre, and spreads outwards towards the periphery. The bilirubin-calcium is dissolved out, and the percentage of cholesterin increases; in this way a pure cholesterin calculus may be produced.

Time Required for the Formation of Calculi.—On experimental grounds Mignot¹ believes that it takes five or six months to form a stratified, well-formed biliary calculus. On the basis of gall-stones found after an attack of typhoid fever in a young woman Hertz² estimated that calculi may be formed in fifty days. Comparative stagnation of bile is necessary, otherwise the soft, immature calculus would be expelled with the bile from the gall-bladder. Calculi in the gall-bladder may be all of the same age and due to a single attack of cholecystitis. In recurrent attacks,—and these readily take place in a damaged gall-bladder,—fresh calculi may be formed. The formation of calculi in the ducts is described on p. 709.

Size and Number.—There may be one or thousands of calculi in the gall-bladder. A single calculus may be very large and cause great distension of the gall-bladder; it is usually a laminated or pure cholesterin stone.

Meckel recorded a calculus $6\frac{1}{2}$ inches long and 6 inches thick. In Fiedler's³ case a calculus weighed $1\frac{1}{2}$ ounces, and consisted of three pieces which fitted together to form a cast of the elongated gall-bladder at least 12 inches long. Nehr Korn⁴ recorded a gall-stone in the gall-bladder weighing just over 3 ounces. Bartlett⁵ removed a calculus weighing $2\frac{1}{2}$ ounces from the common bile-duct of a man aged forty-six; the cavity left in the common duct received the operator's fist. The patient recovered. Richter⁶ in 1793 recorded an enormous calculus weighing 3 ounces 5 drams, which is the largest ever described.

Occasionally the number of small calculi in the gall-bladder is very large. Naunyn⁷ counted 5000 in a gall-bladder, but this is surpassed by ~~7802~~ in ~~Otto's~~ case. The small calculi found in such cases are curiously alike in appearance, and are generally of the mixed cholesterin form.

¹ Mignot, R. *Thèse de Paris*, 1897; and *Arch. gén. de méd.*, Paris, 1898, clxxxii, 129.

² Hertz. *Proc. Roy. Soc. Med.*, 1910, iii (Clin. Sect.), 169.

³ Fiedler. *Jahresb. d. Gesellsch. f. Nat.- u. Heilk. in Dresd.*, 1879.

⁴ Nehr Korn. *Deutsche Ztschr. f. Chir.*, Leipz., 1908, xcvi, 319.

⁵ Bartlett. *Ann. Surg.*, Lond., 1908, xlviii, 676.

⁶ Vide Hutchinson's *Arch. Surg.*, Lond., 1892, iii, 6.

⁷ Naunyn. *On Cholelithiasis*, p. 6. Transl. New Syd. Soc., 1896.

⁸ Otto. Quoted by Thudichum. *A Treatise on Gall-stones*, p. 198, 1863.

omit

Otto 7802

14,000

Schackrey's

Schackrey's

Schackrey, A. Quoted by Chauffard, La lithiase biliaire, p. 63, 1922



Shape.—There is great variation in the shape of biliary calculi; this largely depends on their surroundings. Apart from external influences, calculi tend to be round. The large single stone filling up the gall-bladder is usually somewhat elongated and pear-shaped, and may be conglomerate from the union and welding together of previously separate calculi. A single loose calculus, when composed of pure cholesterolin, is often bossed like a mulberry calculus in the kidney. Multiple gall-stones in the gall-bladder are sometimes round, but are more often irregularly square, with facets separated by rounded edges. When impacted in the commencement of the cystic duct, a calculus may be somewhat elongated. Crumbling calculi in the common bile-duct become elongated and moulded to the duct. The small bilirubin-calcium calculi formed in the intrahepatic ducts are elongated and represent the lumen of the duct in which they were formed. Occasionally branching calculi resembling coral are found in the larger intrahepatic ducts.

Small *facets* on the surface of gall-stones shew that there either are or have been more than one calculus in the gall-bladder or ducts. Two or more facets on one calculus are in favour of the number of stones being more than two. Faceting generally indicates that the calculi have been closely packed. Faceting is commoner on medium-sized stones, but may be seen on comparatively large calculi. In small bilirubin-calcium calculi which are freely movable on each other there are no facets as a rule.

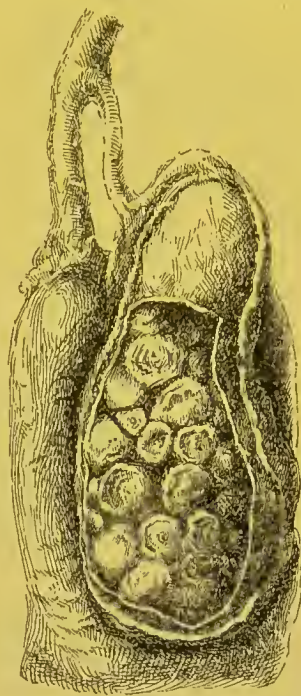


FIG. 103.—Gall-bladder. Distended with faceted gall-stones. In St. George's Hospital Museum, Series ix, 198B. (Drawn by Dr. E. A. Wilson.)

Situation.—Out of 184 cases of cholelithiasis analysed by Kelly,¹ 101 (55·5 per cent) had gall-stones in the gall-bladder alone, 23 (12·5 per cent) in the gall-bladder and cystic duct, 19 (10·5 per cent) in the gall-bladder and common duct, 12 (6·6 per cent) in the common duct alone, and 11 (6 per cent) in the cystic duct alone. Calculi in the gall-bladder are usually loose in the bile, or, when the cystic duct has been permanently blocked for some time, in mucus. In some cases the gall-bladder is firmly contracted on a calculus, or it may contain a large number of calculi closely packed and faceted on each other, there being no bile or mucus in the gall-bladder. When the gall-bladder is thus distended with calculi a crackling sensation may sometimes be felt on palpation. A large number of small stones in inspissated mucus which had acquired the consistency of thick paste and formed a cast

¹ Kelly, A. O. J. *System of Medicine* (Osler and M'Crae), 1908, v, 831.

of the gall-bladder, is figured by Bland-Sutton¹ as "gall-stones in aspie."

A large gall-stone may be adherent to the mucous membrane of the gall-bladder. Calculi in the distal compartment of an hour-glass gall-bladder may be closely united to the mucous membrane. It is comparatively common to find a calculus impacted in the neck of the gall-bladder

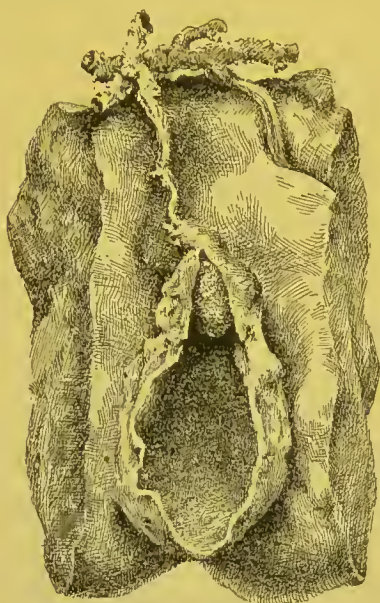


FIG. 104.—A calculus impacted in the neck of the gall-bladder. From a specimen in St. George's Hospital Museum, Series ix, 199A. (Drawn by Dr. E. A. Wilson.)

and thus obstructing the cystic duct. Calculi and masses of cholesterol which hardly deserve the name of calculi are sometimes embedded in the wall of the gall-bladder. Calculi may enter a diverticulum due to ulceration of the gall-bladder, and from subsequent closure of the orifice of the diverticulum become enclosed in the wall of the gall-bladder. Masses of cholesterol may probably be formed from the mucous glands of the gall-bladder.

Peraire² recorded a case with a series of parietal gall-stones embedded in the wall of the gall-bladder, and 27 calculi the size of peas in the lumen of the cystic duct, but none in the cavity of the gall-bladder.

A gall-stone may set up ulceration and weakening of the gall-bladder, and may thus form a diverticulum in which it becomes encysted. This is rare, and is more often seen near the fundus or at the neck of the gall-bladder. Under ordinary conditions the calculi are usually found in the fundus of the gall-bladder.

Calculi in the cystic and common bile-duct are referred to elsewhere (*vide* pp. 745 and 747). In rare instances a calculus derived from the gall-bladder passes backwards from the cystic duct into the common hepatic duct.

Carwardine³ removed gall-stones from the gall-bladder, cystic, common bile, and hepatic ducts of a girl aged seventeen. M. H. Richardson⁴ removed 12 gall-stones from the hepatic duct and 3 from the common bile-duct of a patient who had never shewn a trace of jaundice.

Intrahepatic calculi of large size are very rare; the common and hepatic ducts are usually also full of conerctions.

¹ Bland-Sutton. *Gall-stones and Diseases of the Bile-ducts*, p. 62, 1907.

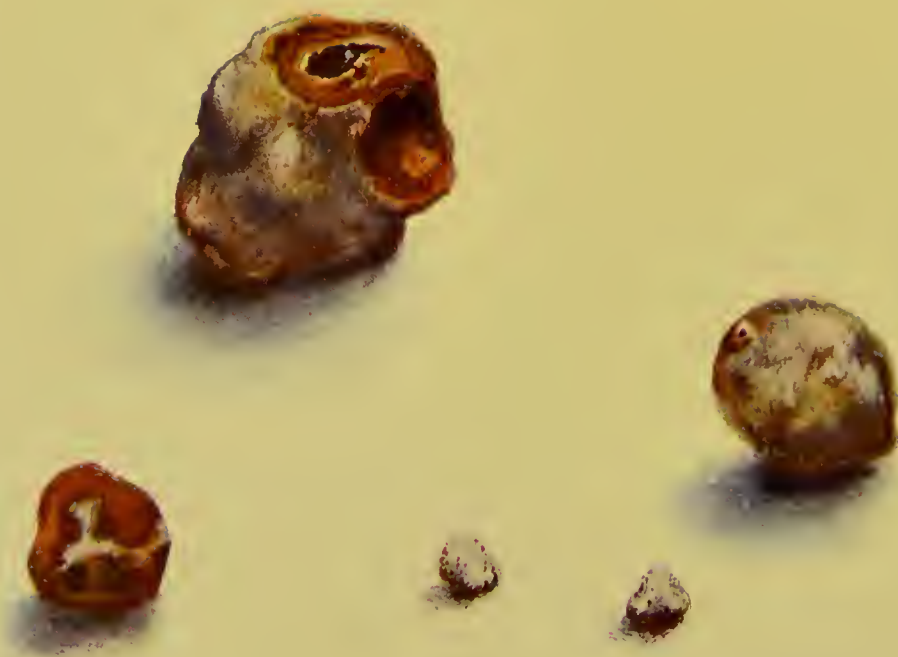
² Peraire. *Bull. Soc. anat.*, Paris, 1902, lxxvii, 707.

³ Carwardine. *Brit. Med.-Chir. Journ.*, 1908, xxvi, 39.

⁴ Richardson, M. H. *Trans. Am. Surg. Assoc.*, 1905, xxiii, 217.

Small calculi may form in
"Luschka's crypts" which form
in chronically infested gall-bladders.

PLATE VI.



GALL-STONES FROM A CASE IN WHICH FRACTURE WAS SPONTANEOUS.

The largest calculus shews surface where spontaneous fracture has occurred. The calculus below and to the left fitted into it. The other calculi were in the same gall-bladder. From a case of primary carcinoma of the gall-bladder in which spontaneous fracture of the calculi had occurred. Painted by Dr. E. A. Wilson.

Lenhartz

Lewishon

Weber

Lenhartz. Quoted by Jacobson. Archives of Surgery
1920, 1, 300

WEBER, F.P. Clin. Journ., London, 1921, 4, 165

Lewishon. Ann. Surg., 1916, LXIII, 525

Thudichum¹ in 1863 collected six cases including Cruveilhier's plate (livraison xii, Plate V), of large branching intrahepatic calculi like coral. I met with one such case in a man who died with diabetes from secondary chronic pancreatitis² (*vide* Fig. 105). There are good specimens of multiple intrahepatic calculi in the museums of the London and Westminster Hospitals (No. 581). In Vachell and Stevens'³ case there was 520 calculi, the largest being $1\frac{3}{4}$ inches long, in the dilated intrahepatic ducts. Other cases have been reported by M'Arthur,⁴ Draper,⁵ and Hawkes.⁶ In the last ^{two} cases the calculi were successfully removed during life. Major Barry sent me notes about a Hindu cook whose common bile, hepatic and intrahepatic ducts were



FIG. 105.—Large intrahepatic calculi distending the right and left hepatic ducts.
(Drawn by Dr. E. A. Wilson.)

distended with small gall-stones. These calculi usually cause jaundice and a good deal of pericholangitis, which may be suppurative. In Draper's case jaundice was absent. The calculi are chiefly composed of bilirubin-calcium. Smaller calculi are not so rare in the intrahepatic ducts; among 72 cases of cholelithiasis collected by Beer⁷ 5 shewed calculi in the intrahepatic ducts. Small black bilirubin-calcium calculi are not uncommon. Occasionally masses of calculous material are found embedded in the substance of the liver in dilated, ampulla-like terminations of bile-ducts which have lost their continuity with the bile-ducts.

Spontaneous Fracture of Gall-stones in the Gall-bladder.—Cases

- ¹ Thudichum. *A Treatise on Gall-Stones*, p. 176, 1863.
- ² Rolleston. *Trans. Path. Soc.*, Lond., 1898, xlix, 133.
- ³ Vachell and Stevens. *Brit. Med. Journ.*, 1906, i, 434.
- ⁴ M'Arthur. *Journ. Amer. Med. Assoc.*, Chicago, 1905, xlv, 1797.
- ⁵ Draper. *Proc. Path. Soc. Phila.*, 1910, N.S., xlii, 16.
- ⁶ Hawkes. *Presbyterian Hosp. Rep.*, N.Y. 1906, vii, 230.
- ⁷ Beer, E. *Arch. f. klin. Chir.*, 1904, lxxiv, 115.

in which a gall-stone has been found to have broken up within the gall-bladder have been reported by Pearce Gould,¹ Hadden,² Calvert,³ and myself.⁴ I have seen one case since the one I reported. Trauma during life or in the course of the post-mortem examination appears to have been excluded, and, though conceivable, it does not seem very likely that vigorous contraction of the gall-bladder would fracture even a friable calculus. Calvert suggested that fracture might depend on drying of a calculus. It is conceivable that in some instances the union and subsequent disruption of a number of calculi might imitate spontaneous fracture. Care must also be taken not to regard as examples of spontaneous fracture marked faceting of the surfaces of adjacent calculi. Probably fracture is brought about in much the same way as spontaneous fracture of calculi in the urinary bladder, as explained by W. M. Ord⁵ and Plowright.⁶ Chauffard⁷ and others have shewn that micro-organisms may also pass into calculi, and by forming a deposit between its layers this microbial invasion would tend to loosen and split off the more superficial strata of the calculus.

CLINICAL PICTURE

Gall-stones are frequently found in the gall-bladder quite unexpectedly. Kehr⁸ states that symptoms occur in only 5 per cent of persons whose gall-bladders contain calculi, but probably this understates the clinical importance of gall-stones, for symptoms really due to cholelithiasis are often regarded as dyspeptic both by the patients and by their medical advisers; further, the presence of gall-stones in the gall-bladder at the necropsy of a patient who has died of some independent disease does not satisfactorily prove that there have never been any symptoms due to gall-stones, ~~as the history may well be deficient. When gall stones are found during the course of an abdominal operation enquiry will often elicit a history of symptoms pointing to their presence.~~ Moynihan⁹ has found this universally. Latency is especially common in old people, in whom the muscular tissue of the gall-bladder and ducts is atrophied, and it has been thought that for this reason the passage of a calculus out of the gall-bladder into the ducts is less likely to occur.

The symptoms produced by gall-stones are extremely numerous and variable. It is difficult to divide the symptoms satisfactorily into water-tight groups, for there is a certain amount of overlapping. I propose to

¹ Pearce Gould. *Trans. Clin. Soc.*, Lond., 1888, xxi, 193.

² Hadden. W. B. *Trans. Path. Soc.*, Lond., 1890, xli, 160.

³ Calvert, J. *Ibid.*, 1898, xlix, 139.

⁴ Rolleston, H. D. *Ibid.*, 1898, xlix, 135.

⁵ Ord, W. M. *Ibid.*, 1877, xxviii, 170; 1881, xxxii, 304.

⁶ Plowright. *Ibid.*, 1896, xlvii, 132.

⁷ Chauffard. *Rev. de méd.*, Paris, 1897, xvii, 81.

⁸ Kehr, H. *Diagnosis of Gall-stone Disease*, p. 25, American transl., 1901.

⁹ Moynihan. *Brit. Med. Journ.*, 1908, ii, 1599.

1 } and in 1920 Jewell & Barker raised this
estimate to 10 per cent

Ingraham is emphatic that all gallstones, except pure cholesterol
calculi, cause symptoms
and W. J. Mayo expressed his view in
the title of a paper "Benign gallstones a myth"

Barker, L. F. Journ. Amer. Med. Assoc., Chicago, 1920, Lxxvi, 1108
Mayo, W. J. Journ. Amer. Med. Assoc., Chicago, 1911, Lvi, 1021

may come on directly
after a meal, but more
often are delayed for 3 or
more hours and so
imitate duodenal
ulcer.

numbness of the right arm, after or independently of
pain, slight paresis of arm associated with hepatic pain,
and febrile attacks with urrobilinuria after jolting
(Fournier) are other manifestations

BAHRDT ~~has drawn~~ ^{described} attention to cases
of gall-stones ^{bladder disease} and cholecystitis in which
attacks of fever are associated with bronchitis
or signs suggesting pneumonia; ^{and} subsequently, ^{short}
~~the attacks are~~ ^{complicated} with jaundice; The
pulmonary manifestations ^{being regarded} are ^{thought to be} as
due to infection from the latent cholecystitis.

Fournier, J. c. m. Bull. et mem. Soc. Méd. des hôp. de Paris,
1924, 3^e ser., XLVIII, 1742

Bahrcht. München. med. Wchnschr., 1912, LIX, 2326

consider them under the following heads: (I) Masked or inaugural symptoms; (II) biliary colic; (III) the purely mechanical or aseptic effects of gall-stones; (IV) the inflammatory and infective changes set up by cholelithiasis; special descriptions will be given of intestinal obstruction and of fistulae produced by gall-stones, under the headings (III) and (IV) respectively.

I. MASKED OR INAUGURAL SYMPTOMS.—The symptoms accompanying the presence of gall-stones may not be characteristic, and it has long been recognised that "dyspepsia" may disappear after removal of gall-stones. These symptoms ~~have been~~ called "inaugural" by Moynihan¹ who insists, contrary to Kehr, that gall-stones always cause symptoms. These early symptoms are flatulence, fulness and dull pain in the epigastrium ~~coming on about half an hour after meals or~~ in the middle of the night, and specially induced by certain forms of food, such as apples and cheese. In these attacks, which are relieved by eructations or vomiting, but not by taking food, there may be pain resembling that of pleurisy due to spasm of the diaphragm. There may also be slight shivering of short duration, drowsiness, and headache. The "goose-skin" sensation is allied to the more pronounced feverish attacks in intermittent hepatic fever (p. 759). There may be chronic pain in the back imitating lumbago, or pain on the top of the right shoulder passing down the outside of the arm which may for years be regarded as neuritis (Mackenzie²). It is important to recognise these early manifestations of gall-stones, but Moynihan and Sherren³ both agree that a diagnosis between these manifestations of gall-stones and ulcer of the stomach and duodenum may be impossible.

II. BILIARY COLIC is generally regarded as the result of spasm excited by the passage of a calculus down the bile-ducts. Attacks of pain of less severity may possibly be due to spasm set up by a stone in the gall-bladder which has not actually entered the cystic duct. Inspissated bile and masses of precipitated cholesterin and bile-pigments in the ducts may also induce biliary colic. Inflammation and spasm extending to the ducts from cholecystitis must also be reckoned with as a cause of biliary colic. In other words, biliary colic may, like the pain of appendicitis, be independent of calculi. Cholecystitis with closure of the cystic duct will cause painful contractions of the gall-bladder; in many cases the factor responsible for closure of the cystic duct is a calculus. According to Lennander⁴ spasm of the gall-bladder and bile-ducts is not painful *per se*, but only because it causes traction on the sensitive subperitoneal tissues. Some writers, such as Riedel⁵ and Kehr,⁶ minimise the mechanical rôle of calculi in biliary colic, and insist on the import-

¹ Moynihan. *Brit. Med. Journ.*, 1908, ii, 1598; *Practitioner*, Lond., 1908, lxxxii, 830.

² Mackenzie, J. *Symptoms and their Interpretation*, ed. 2, p. 159, 1912. Lond.

³ Sherren. *Lancet*, Lond., 1911, ii, 870.

⁴ Lennander. *Hygiea*, Stockholm, 1907, 2. f., vii, 657.

⁵ Riedel. *Berlin. med. Wchnschr.*, 1901, xxxviii, 1.

⁶ Kehr, H. *Diagnosis of Gall-stone Disease*, p. 26, Amer. transl., 1901.

largely due
to air
swallowing

particular

ance of cholecystitis and on the extension of inflammation to the ducts as the cause of pain and jaundice. But though inflammatory obstruction of the cystic duct is quite enough to set up painful contractions of an inflamed gall-bladder, there is no reason to doubt that the mechanical irritation of a calculus in the ducts sets up spasm and colic in the same way that a calculus in the ureter causes renal colic. In other words, biliary colic may be due to inflammatory or to mechanical obstruction, or to both combined.

Cause of the Passage of Calculi out of the Gall-bladder.—As gall-stones are commonly latent in the gall-bladder, some conditions other than those of ordinary life must be responsible for the passage of calculi into the cystic duct, and something more is required than the ordinary contractions of the gall-bladder which suffice to drive out the bile. It has been thought that unusually vigorous contractions of the gall-bladder, such as might be induced by violent emotion, may determine the passage of gall-stones into the cystic duct. The onset of colic at the menstrual periods has been referred to spasmodic contraction of the gall-bladder set up by nervous perturbation and general abdominal hyperaemia (Cornillon¹). Occasionally jolting, such as riding in a cart without springs, a railway journey, or bicycling, has been thought to determine the passage of calculi into the cystic duct. Keay² believes that pain following jolting is due to stretching of adhesions rather than to the passage of gall-stones, and that a stooping posture favours the migration of a calculus out of the gall-bladder. Palpation of the gall-bladder is certainly sometimes followed by colic, but it can be very rarely that the stone is directly forced into the cystic duct. Von Noorden³ has pointed out that biliary colic may occur in patients immediately after treatment for obesity, and suggests that the removal of fat allows the pressure of corsets to interfere with the flow of bile out of the gall-bladder.

While not denying the possibility that the contractions of the gall-bladder may drive calculi into the cystic and common bile-duct, Kehr⁴ believes that the important factor in determining the migration of calculi from the gall-bladder into the ducts is inflammation of the gall-bladder. The mechanism is as follows: Cholecystitis gives rise to an inflammatory exudation which distends the gall-bladder and drives the calculus into the cystic duct. Enlargement of the gall-bladder, tenderness, and fever during biliary colic are in favour of the view that cholecystitis plays an important part in its production. When the calculus is impacted in the duct, it will mechanically set up painful spasm of the ducts and gall-bladder. Acute cholecystitis may be set up by infection either from the intestine or from the general circulation. Diarrhoea, typhoid fever, and influenza, may thus precede an attack of biliary colic. Trauma, such as a fall or blow, may, by reducing the

¹ Cornillon. *Progrès méd.*, Paris, 1897, 3. s., v, 257.

² Keay. *Medical Treatment of Gall-stones*, p. 37, 1902.

³ Von Noorden, C. *Diseases of the Metabolism and Nutrition*, part i, Obesity, p. 31, 1903. E. B. Treat and Co., New York.

⁴ Kehr. *Loc. cit.*, p. 26.

, and shoulder blade / n

FRischmann / n

FRischmann, E.S. Brit. med. Journ., 1923, II, 811

resistance of the gall-bladder, allow micro-organisms to set up cholecystitis and so lead to the expulsion of a calculus into the ducts.

The onset of biliary colic may be quite sudden, or may be preceded by symptoms, such as shivering, nausea, and vomiting, compatible with the view that cholecystitis is in progress. Formerly the entrance of a gall-stone into the cystic duct was thought to be due to contractions of the gall-bladder set up reflexly by the passage of food into the duodenum, and three to four hours after a meal was thought to be a specially probable time for the onset of biliary colic. Biliary colic more commonly commences at night.

~~The onset of the menstrual period has been thought to determine an attack of biliary colic.~~ Biliary colic may occur at any period during pregnancy, but during lactation it is either less frequent or absent. After weaning the child, however, severe attacks may occur. After delivery conditions leading to infection of the gall-bladder are not uncommon, and thus the onset of colic may be determined.

Signs and Symptoms.—The *pain* in biliary colic is due to two factors: in the first instance, there is probably nearly always acute inflammation of the gall-bladder; secondly, the muscular spasm set up by the presence of the calculus in the duct. The pain of acute cholecystitis is felt in the right hypochondrium and epigastrium. The entrance of the calculus into the cystic duct sets up severe muscular spasm and pain in the right loin, ~~and~~ back. Keay,¹ from personal experience and from observation of patients, believes that pain due to a calculus in the cystic duct begins to the right of the region between the eighth and eleventh dorsal vertebrae. ~~In this view Keay differs from most authorities, such as Naunyn, who state that the pain begins in the epigastrium or right hypochondrium. This pain is extremely severe, as if the back was being broken. It passes to the right hypochondrium and radiates from this spot in all directions—to the left hypochondrium, the umbilical and hypogastric regions, to the thighs, and even to the arms and neck. The pain may radiate to the right shoulder, but this is less frequent in biliary colic than in hepatic abscess. In rare instances the pain is referred to the left side; ~~two~~ cases of transposition of the viscera have been operated upon for gall-stones (Beck,² Billings³). Mayo Robson⁴ observed left-sided pain in cases in which subsequent operation shewed adhesions between the pylorus and the gall-bladder.~~

-d)

Keay's

In one case attacks of colic followed by the passage of small calculi, which I examined, were limited to the epigastrium and left side. There was no transposition of the viscera, but more than twenty years ago the patient had had a right-sided empyema drained, with, however, very little thoracic deformity. I have also seen it in a woman who had had much pelvic inflammation on the left side.

¹ Keay. *Medical Treatment of Gall-stones*, p. 75, 1902.

² Beck. *Ann. Surg.*, 1899, xxix, 593.

³ Billings. *Phila. Med. Journ.*, 1900, vi, 670.

⁴ Mayo Robson. *System of Medicine* (Allbutt and Rolleston), 1908, iv, part i, 259.

The pain, which is usually paroxysmal, is probably one of the worst that afflict humanity; women speak of it as being much worse than the pains of labour. It may be so intense as to cause hysterical or epileptiform attacks, and in very rare cases the patients have died, apparently simply from shock (*vide* p. 735). The pain is so excruciating that the patient throws himself into various positions to obtain relief, but without any success. He may roll in agony on the floor and scream, cry, or groan in a very distressing manner. The severity of the pain gradually diminishes, and leaves a constant dull aching which is interrupted by acute paroxysms. The first is nearly always much worse than subsequent seizures, and in a first attack a small calculus may give rise to far more pain than larger gall-stones on later occasions. There is thus no absolute relation between the size of the calculi and the severity of the pain. The ducts become dilated by the passage of successive calculi, and eventually a large one may pass almost unnoticed. Pain may suddenly disappear as if by magic; this may be explained as due to sudden relief of tension in the gall-bladder from removal of obstruction, for example the escape of the calculus into the gall-bladder or the duodenum. Keay believed that at the moment when the stone passes into the duodenum there is a peculiar gliding sensation to the right of the tenth and twelfth dorsal vertebrae. The violent pain usually lasts for some hours—three to twelve—if unrelieved by morphine; in rare instances for a few minutes only. Severe pain is sometimes described as lasting for days, but this is probably due to a succession of attacks supervening rapidly, with slighter pain, due to the inflamed or distended and inflamed gall-bladder, in the intervals between the more severe paroxysms. Cutaneous hyperalgesia is described by Head¹ in the eighth dorsal segment and may occur on both sides. ~~(After the subsidence of the attack)~~ the skin and muscles on the right side of the abdomen may be tender for weeks (Mackenzie²).

It has been estimated that the temperature is raised in 60 per cent of the cases. The fever is explained by the concomitant cholecystitis or cholangitis; in some instances a palpable and tender gall-bladder, splenic enlargement, and albuminuria lend support to the theory of infection. The fever was formerly thought to be reflex, and due to the violent nervous stimuli accompanying the colic. This view is to some extent supported by cases in which at operation there is no manifest inflammation of the gall-bladder or ducts. But in such cases it is not unreasonable to believe that there is infection sufficient to induce fever, though not to produce naked-eye changes.

Boix³ suggested that during biliary colic the detoxicating function of the liver is suspended and that toxins absorbed from the intestinal tract thus pass into the general circulation and give rise to pyrexia.

¹ Head. *Brain*, Lond., 1893, xvi, 73.

² Mackenzie. *Symptoms and their Interpretation*, ed. 2, pp. 48, 159, 1912, Lond.

³ Boix, E. *Arch. gén. de méd.*, Paris, 1901, clxxxviii, 466.

have been described (Chauffard)

in the intervals ~~between~~ as many as eight tender spots, namely
the epigastrium, over the gall bladder, ~~the~~ the intra-pancreatic part, of
the common bile duct, the tip of the right 11th rib, the right phrenic
^{below the 2nd head of the elevator scapulae} nerve, the right shoulder, the inferior angle of the right scapula, the
angle of the right scapula, & the spine of the 8-11 dorsal vertebrae.

in
due to some cases
to swallowing
air, }

Hofmeister, Zentr. f. Klin. Med.
1912, cviii, 255

Reflex vomiting accompanies the intense pain, and is often followed by some relief. The contents of the stomach are first brought up, and subsequently those of the duodenum; in very rare instances a calculus has been vomited (*vide* p. 769). There is usually bile in the vomit, which suggests that at this period the common duct is not completely occluded. Dyspepsia and flatulence may accompany or follow the attack. The amount of active hydrochloric acid in the gastric juice is diminished during the attack, but increased in the intervals (Lichty¹). There is naturally distaste for food, though thirst may be urgent. Constipation is usually present. With well-marked jaundice the faeces may be colourless, but this is far from constant. The abdomen is usually somewhat retracted from vigorous contraction of the abdominal muscles. Occasionally there is considerable tympanitic distension, but, according to Naunyn, this is seen only in persons habitually flatulent. Transient dilatation of the stomach has been described.

The liver is enlarged in some instances, according to Kehr, in from 10 to 20 per cent, but this is difficult to determine, as the hypochondrium is extremely tender and the patient, being in great pain, is naturally far from tolerant of examination, and the recti are rigid. The swelling of the liver may be partly due to inflammation of the bile-ducts and partly to retention of bile from the obstruction. It is often tender without any manifest enlargement. The gall-bladder is probably frequently enlarged, but its examination is far from easy, as there are usually considerable tenderness over the gall-bladder and rigidity of the abdominal muscles. Naunyn estimates that the gall-bladder is only palpable in one-third of the cases of biliary colic.

Enlargement of the spleen is also difficult to estimate, but probably only occurs when severe infective processes or other complications are present. Gilbert and Lereboullet,² however, suggest that during biliary colic the pressure of bile in the intrahepatic ducts may compress the branches of the portal vein and give rise to passive engorgement and splenic enlargement.

During a paroxysm the skin is hot and moist or bathed in perspiration, and there may be rigors or shivering. The intense pain leaves considerable prostration for a time after the paroxysm has passed off. Nervous symptoms occasionally accompany biliary colic and are due to the intense visceral pain. Hysterical manifestations,³ epileptiform convulsions, or even angina pectoris (Douglas Powell⁴) may occur. Sudden death during a paroxysm of pain, due to cardiac inhibition brought on reflexly through the vagus, has been recorded in rare instances.

Naunyn⁵ refers to 9 cases of death during severe biliary colic; Clifford

¹ Lichty. *Amer. Journ. Med. Sc.*, Phila., 1911, cxli, 72.

² Gilbert et Lereboullet. *Rev. de méd.*, Paris, 1904, xxiv, 908.

³ Jeanselme et Rabé. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1898, 3. s., xv, 602.

⁴ Powell. *System of Medicine* (Allbutt and Rolleston), 1909, vi, 188.

⁵ Naunyn. *Cholelithiasis*, p. 89, transl. New Sydenham Soc., 1896.

Allbutt,¹ Osler,² Mayo Robson,³ Calvert,⁴ and Périér⁵ refer to similar cases.

In exceptional instances temporary hemiplegia, paraplegia, or even tetany has been observed. Sleepiness and drowsiness may follow biliary colic and be due to nervous exhaustion, to the presence of bile in the circulation, or in some degree to the morphine. Extreme drowsiness was a striking feature in a woman aged thirty who had suffered from gall-stone colic for six years (Lévi⁶). Kehr⁷ states that the subjects of gall-stone colic frequently have attacks of migraine, which, however, disappear when the calculi are removed by operation. During biliary colic hiccup may occur, and there may be a dry cough due to reflex irritation. Reflex constriction of the vessels in the lungs with rise of blood-pressure in the pulmonary artery, as shewn by accentuation of the pulmonary second sound, has been described, and is supported by the experimental observation that irritation of the bile-duct induces constriction of the pulmonary vessels (François-Franck and Arloing). Signs of congestion of the base of the right lung, and, in very exceptional instances, haemoptysis (Cassoute⁸), have been observed. Dilatation of the right side of the heart has been described, and has been referred by Potain to the rise of pulmonary blood-pressure. It may also be due in some measure to poisons absorbed from the bile-ducts, or in some cases to the effect of bile salts. Temporary dilatation of the left ventricle with a systolic apical murmur may also occur (Gangolphe,⁹ Riesman), and has been ascribed to the influence of the high blood-pressure caused by the pains acting on a myocardium weakened by toxæmia. Among 56 gall-stone cases 6, or 10·7 per cent, had transient murmurs (Riesman¹⁰).

There may be palpitation, disturbed cardiac rhythm, with rapid action, irregularity, or even slowing of the heart. The pulse during a paroxysm becomes small, feeble, and is generally of about the normal rate; in some cases it is even slower than normal. Kraus¹¹ observed a pulse of 42 in one case.

A moderate degree of leucocytosis in severe biliary colic, to about 15,000, is very common (Emerson¹²). Albuminuria is not infrequent. There is some difference of opinion as to the frequency with which glycosuria occurs. It has been referred to the widespread nervous disturbance, but it is conceivable that it is toxic. True diabetes may be the result of chronic pancreatitis set up by a calculus in the lower part

¹ Allbutt. In *System of Medicine*, 1907, iii, 304.

² Osler. *Principles and Practice of Medicine*, p. 551, ed. vi, 1905.

³ Mayo Robson. *Gall-stones*, p. 77, 1892.

⁴ Calvert, J. T. *Ind. Med. Gaz.*, 1903, xxxviii, 413.

⁵ Périér. *Normande méd.*, 1904, xix, 396.

⁶ Lévi. *Arch. gén. de méd.*, 1896, clxxvii, 63.

⁷ Kehr. *Diagnosis of Gall-stone Disease*, p. 56, American transl., 1901.

⁸ Cassoute. *Bull. méd.*, Paris, 1897, xi, 821.

⁹ Gangolphe. *Thèse de Paris*, 1875.

¹⁰ Riesman. *Amer. Journ. Med. Sc.*, Phila., 1911, cxlii, 655.

¹¹ Kraus. *On Gall-stones*, p. 36, English translation, 1896.

¹² Emerson. *Clinical Diagnosis*, p. 586, 1906.

W. Russell

From immobilization of the right half
of the diaphragm the breath sounds over
the right chest are often deficient (Ramead, Vincent and Clément)

Tenderness on the right side
between the 2 heads of the
sterno-mastoid muscle has
been described (Cade and Passier)

From chronic infection of the ~~conduits~~ ^{auricular} ~~auricular~~ ^{and cardiac} ~~and cardiac~~ ^{fibrillation}
gall bladder myo-carditis may
result.

Russell, W. The Stomach and Abdomen, p. 257, 1921

Ramead, Vincent et Clément. Bull. et mém. Soc. méd. des hôp. de Paris 1920, 3^e sém. XLIV, 117

Cade et Passier Revue méd., Paris, 1919, XXXVI, 475.

Hansen regarded urobilinogenuria
as ~~the~~ constant, but this is
denied by Meulengracht

It may be occult and proved
only by estimation of the
bilirubin content of the plasma.

Hansen, S. Agesk. f. Læger. 1920, ⁽⁸²⁾ Lxxxii, 415
Meulengracht, E. Arch. Int. Med., Chicago, 1925, xxv, 214

of the common bile-duct, but these patients are not often the subjects of typical biliary colic. Conversely in two well-marked cases of diabetes mellitus Gilbert and E. Weil¹ observed that during intercurrent attacks of hepatic colic the glycosuria diminished. Bile-pigment occurs in the urine before there is any manifest jaundice; the presence of bile in the urine may be quite transient and may be succeeded by an excess of urobilin; Indican does not occur in uncomplicated cases; this is a point of importance in distinguishing biliary from appendicular and intestinal colic in which indican may be present.

Jaundice is not an invariable accompaniment of biliary colic. Its incidence has been variously estimated at one-half to three-quarters of all the cases. In the higher estimate cases of very slight and transient icterus are included. Naunyn² considers that definite jaundice is present in half the cases. It comes on a varying time after the onset of the pain, and no constant interval can be given. It may vary between a few hours to two or even three days. The occurrence of jaundice after biliary colic is the result of obstruction to the flow of bile through the common bile-duct. The obstruction is generally assumed to be due to the presence of the calculus in the duct, but it may be due to the spread of inflammation and spasm from the gall-bladder to the ducts, and may occur when the calculus is still in the gall-bladder or in the cystic duct. Riedel believes that two-fifths of the cases of jaundice in cholelithiasis are due to this cause. The conjunctivae become yellow before the skin.

During an attack of gall-stone colic not only is no food taken, but the vomiting and fever lead to temporary loss of flesh and weight. When attacks are repeated, nutrition may become very seriously affected.

Complications.—The extremely forcible peristaltic contractions of the intestines, set up reflexly during the height of biliary colic, may cause volvulus of the small intestine and so acute intestinal obstruction (Mayo Robson³). Intestinal obstruction produced by gall-stones in other ways, viz. by mechanical obstruction of the lumen of the bowel, by a large calculus, as the result of local peritonitis around the gall-bladder, and by adhesions, is referred to elsewhere (*vide* pp. 751, 758).

Rupture of the gall-bladder or ducts during an attack is fortunately very rare; when it occurs, infection of the peritoneum with fatal results is very prone to occur.

Pauly⁴ describes a case in which, after an attack of biliary colic, collapse, abdominal distension, and death occurred. Blood clot was found in the abdomen. There was rupture of the capsule of the liver leading into a cavity containing blood. There were calculi in the gall-bladder and a calculus obstructing the common duct.

The cholecystitis which probably always precedes and gives rise to

¹ Gilbert et Weil. *Bull. et mém. Soc. méd. des hôp. de Paris*, 1898, 3 s., xv, 633.

² Naunyn. *Cholelithiasis*, p. 76. Transl. New Sydenham Soc., 1896.

³ Mayo Robson. *Med.-Chir. Trans.*, Lond., 1895, lxxviii, 117.

⁴ Pauly. *Lyon méd.*, 1892, lxx, 430.

biliary colic may become suppurative, or even perforate and set up peritonitis.

Termination.—An attack of biliary colic may terminate suddenly, the pain disappearing in a moment, probably from the calculus dropping back into the gall-bladder or escaping into the duodenum. In other cases the pain may recur at frequent intervals, the calculus, or possibly a succession of calculi, being finally discharged into the duodenum. There is not any convincing evidence that recurring attacks of colic without jaundice are due to a calculus which has once passed into the cystic duct, returning to the gall-bladder and entering the cystic duct again and again. Possibly some of these cases are due to cholecystitis alone, and others to pancreatic lithiasis. The calculus may become impacted close to the biliary papilla and produce intermittent hepatic fever (*vide* p. 759). In rare instances death may occur from various causes. The pain may be so intense that death results from reflex cardiac inhibition (*vide* p. 735). Death from peritonitis due to rupture or ulceration of the ducts or gall-bladder is also described.

Diagnosis.—The extremely severe pain in the right hypochondrium and back, the tenderness over the gall-bladder between the ninth costal cartilage and the umbilicus, vomiting, the subsequent appearance of jaundice, though this is not essential, and the recognition of gall-stones in the stools are the chief points on which a diagnosis of gall-stone colic rests. The presence of calculi in the faeces of course clinches the diagnosis, but calculi are by no means always found; according to Kehr in not more than 25 per cent. The motions should be passed into a solution of carbolic acid 1 : 60, and broken up with the aid of a piece of stick and passed through a sieve.

The patient may be in such agony that it may be very difficult, especially in a first attack or when first seen, to make out what is the matter. In such cases a hypodermic injection of morphine will enable an investigation and a diagnosis to be made. A few whiffs of chloroform remove the widely spread pains and leave a subdued ache in the region of the gall-bladder.

Differential Diagnosis from Cholecystitis.—In acute cholecystitis without gall-stones the pain may be so severe as to imitate colic due to a calculus; Sheldon¹ has collected 32 cases in point. Moreover, it is probable that acute cholecystitis is antecedent to the onset of calculous colic (Kehr,² Naunyn³). The chief distinction between the two is the greater severity of the pain in gall-stone colic, but this criterion often fails us.

Renal Colic.—Since the pain due to a calculus in the cystic duct is felt to the right of the spine opposite the eighth to eleventh dorsal vertebrae, it is not surprising that cases of biliary colic are from time to time diagnosed as renal colic due to a calculus in the right kidney. In renal colic the pain tends to radiate down the ureter instead of forwards

¹ Sheldon. *New York Med. Journ.*, 1905, lxxxi, 69.

² Kehr. *Gall-stone Disease*, p. 26, American transl., 1901.

³ Naunyn. *On Cholelithiasis*, pp. 113-125. Transl. New Sydenham Soc. 1896.



towards the epigastric and hypochondriac regions, while the kidney is tender on palpation in the loin, and the urine may contain blood, pus, or albumin, and is free from bile. The diagnosis of cholelithiasis in early life is difficult, as it is hardly likely to be thought of in the absence of jaundice. The abdominal pain will probably be referred to intestinal disturbance. In this respect cholelithiasis resembles renal colic in infants, which, as Gibbons¹ has shewn, is very likely to be overlooked.

Floating Kidney.—As described elsewhere (p. 555), a floating kidney on the right side may cause biliary colic and jaundice. The diagnosis depends on the detection of a floating kidney and on disappearance of the symptoms when nephroptosis has been efficiently treated either by a belt and pad or by the operation of nephropexy. If attacks of jaundice and colic still continue, it is probable that there is cholelithiasis in addition; in 13 cases of floating kidney with symptoms suggesting cholelithiasis, 2 were found to have gall-stones (Sherren²).

Gastric and Duodenal Ulcer.—The pain due to biliary colic is often regarded not only by the sufferers, but also by their medical advisers, as due to disease of the stomach, such as ulcer, or to a duodenal ulcer. The pain of frank biliary colic is very much more severe than that due to gastric ulcer. In gastric ulcer the pain is chiefly in the epigastrium, and the vomited matters shew excess of hydrochloric acid, whereas in biliary colic the amount of hydrochloric acid is either normal or diminished. Fever, sweating, and prostration are in favour of biliary colic.

Duodenal ulcer is twice as common in men as in women. The pain is relieved by food or by an alkali. Haematemesis may occur or there may be melaena without haematemesis. When the ulcer is in the second part of the duodenum, a rare position, the symptoms may exactly imitate gall-stones (Sherren). The pain of biliary colic is much more severe than that of duodenal ulcer, and is not relieved by taking food or an alkali.

Acute Dyspepsia.—In acute gastritis with flatulent distension of the stomach the symptoms are less urgent than in biliary colic, and there is tenderness over the stomach rather than over the gall-bladder.

Hyperchlorhydria.—In some cases of hyperacidity of the gastric juice attacks of pain may wake the patient up at 3 a.m., and be regarded as due to biliary colic. Examination of the gastric juice and the relief obtained after taking a powder composed of bicarbonate of sodium and carbonate of magnesium should indicate the true nature of these cases.

Appendicitis.—In some cases the pain is referred to the right iliac fossa and the condition resembles appendicitis. A possible explanation of this is that local peritonitis has spread from the gall-bladder to the serous coat of the appendix (Tripier and Paviot³). Ordinary cholecystitis is more likely to resemble appendicitis than is typical biliary colic in which the pain is much more severe and higher

¹ Gibbons, R. A. *Med.-Chir. Trans.*, Lond., 1896, lxxix, 41.

² Sherren. *Lancet*, Lond., 1911, i, 870.

³ Tripier et Paviot. *Semaine méd.*, Paris, 1903. xxiii, 29.

up in the abdomen. But appendicitis and cholelithiasis may coexist (*vide* p. 716).

Mucous Colitis.—When the attacks of abdominal pain in mucous colitis are sufficiently severe to suggest biliary colic, examination of the stools should lead to the detection of the characteristic casts of mucous colitis. It is worth while pointing out that membranous cholecystitis with attacks of biliary colic has been reported in patients with mucous colitis (*vide* p. 614). Mucous colitis may be associated with the passage of intestinal sand and with abdominal pain.

Intestinal lithiasis occurs in two forms: (i) The false—or food residues, such as the sclerenchyma of fruits, especially the pips of pears, the vertebrae of sardines, or drugs, such as magnesia or salol. Olive oil taken by the mouth to relieve cholelithiasis, may be passed as saponified masses, which, from a superficial examination, may be regarded as softened calculi.¹ When colic from other causes, such as constipation, is followed by the passage of these food residues, a diagnosis of biliary sand might easily be made unless the masses are chemically or microscopically examined. (ii) True intestinal sand is composed of calcium phosphate, and is probably the result of a “lithogenic catarrh” of the intestine. It may also contain urobilin. The presence of true intestinal sand is often associated with mucous colitis. In some, but not in all, cases of true intestinal sand there are attacks of severe abdominal pain. A chemical examination of the sand is necessary to distinguish the condition from biliary colic due to minute calculi.

Epigastric hernia with adherent omentum in rare cases imitates biliary colic; possibly the traction exerted on the gall-bladder and bile-ducts acts in the same way as a floating kidney. Lothrop² refers to 6 cases of this nature.

In *acute pancreatitis* there is more profound collapse; the pain is more in the epigastrium, and is more intense and constant than in biliary colic. Acute pancreatitis may follow on biliary colic, and the haemorrhagic form may be due to bile passing into the pancreatic duct when the orifice of the biliary papilla is blocked by a small calculus (Opie³).

Pancreatic colic due to calculi in Wirsung's duct may imitate biliary colic without jaundice. The diagnosis of pancreatic lithiasis is suggested by the discovery in the stools of calculi composed of carbonate and phosphate of lime (*vide* also p. 751).

Hepatic Crises in Tabes, etc.—Crises resembling biliary colic are very rare in tabes, but the resemblance may be very close. Krauss⁴ records a case of a woman aged forty-four who was the subject of tabes and had recurring attacks of colic and jaundice. At the necropsy the gall-bladder and ducts were healthy and free from calculi.

The obscure condition *hepatalgia*, or neuralgia of the liver, has been

¹ Compare Delépine, S. *Trans. Path. Soc.*, Lond., 1890, xli, 111.

² Lothrop. *Boston Med. and Surg. Journ.*, 1897, cxxxvi, 203.

³ Opie, E. L. *Johns Hopkins Hosp. Bull.*, Balt., 1901, xii, 179.

⁴ Krauss. *Journ. Nerv. and Ment. Dis.*, 1899, xxvi, 107.

and Parturier has reported cases in which ~~the~~ biliary colic appeared to be a manifestation of anaphylactic shock.

but is not necessarily relieved by vasodilators and is associated with nausea (Liam, Weissenbach and Parturier).

Faulkner, Marble and White have compared the symptoms of 30 cases of coronary obstruction with those of 30 consecutive cases of of cholelithiasis confirmed by operation; radiation to the arms is in favour of ^{angina} ~~gallstones~~, to the back of gallstones; a feeling of constriction is confined to coronary obstruction.

Parturier, S. Presse med., Paris, 1924, xxii, 849.

Gibson, J.H. Booster med. and Surg. Journ., 1913, CLIX, 861.

Liam, Weissenbach, and Parturier. Presse med., 1924, xxii, 9

Faulkner, J.M., Marble, H.C., and White, P.D. Journ. Amer. Med. Assoc., 1924, LXXXIII, 208

described by Clifford Allbutt¹ and Pariser,² the latter of whom has reported 7 cases of nervous hepatic colic. The patients are neurotic or neurasthenic, but these conditions of course in no way protect against cholelithiasis. Osler³ speaks of pseudobiliary colic as not uncommon in nervous women, and as being periodic and often excited by emotion, but not accompanied by jaundice. The abdominal crises of angioneurotic oedema may simulate recurrent biliary colic (Harrington⁴).

From enteralgia, or *neuralgia of the abdominal sympathetic*, the diagnosis is not always easy. According to Clifford Allbutt,⁵ the pain of enteralgia often begins at the navel and is more stabbing than in biliary colic. In the early stages of an *aneurysm of the abdominal aorta* near the coeliac axis, before pulsation is manifest, attacks of severe pain may suggest biliary colic. Pseudo-gall-stone colic may occur in malignant disease involving the ducts and in malignant disease of the head of the pancreas, but there is such deep jaundice and the condition of the patient is so grave that little or no difficulty in eliminating ordinary biliary colic is likely to arise.

Lead colic, when severe, superficially resembles gall-stone colic in the great abdominal pain and difficulty in making a thorough examination of the patient. The blue line on the gums, the anaemia, and the absence of any localisation of tenderness near the gall-bladder point to lead colic. I have seen recurrent attacks of colic with slight jaundice in workers in lead, suggesting that spasmodic contraction of the bile-ducts, analogous to intestinal colic, may be set up by lead.

Angina Pectoris. The severity of the pain ^{of biliary colic} may, ^{be} when it is referred to the cardiac region, imitate angina pectoris (Gibson).

In a case of de Havilland Hall's⁶ there were attacks of pain in the cardiac region, followed by faintness, which resembled angina but were not relieved by nitrites. Subsequently unmistakable biliary colic, followed by a broncho-biliary fistula, developed and the aberrant pain disappeared.

Lumbago.—The pain in the back with which biliary colic may begin, in some cases, lead to an erroneous diagnosis of lumbago or of spinal disease.

Prognosis.—Under this heading recovery from the actual attack and the prospect as regards the future require consideration.

Death during an attack of biliary colic is extremely rare. It may be due to the intensity of the pain causing cardiac failure (*vide* p. 735), or to rupture of the gall-bladder or bile-ducts during severe spasm, and perforative peritonitis set up by the infected bile. Courvoisier⁷ collected 41 examples of this result.

¹ Clifford Allbutt. *Visceral Neuroses*, 1884; and his *System of Medicine*, 1897, iii, 481.

² Pariser. *Centralbl. f. inn. Med.*, 1896, xvii, 467.

³ Osler, W. *Practice of Med.*, p. 531, 6th ed., 1906. ¹²

⁴ Harrington. *Clinical Contributions, Massachusetts General Hosp.*, 1906, i, 94.

⁵ Clifford Allbutt. *Allbutt's System of Medicine*, 1897, iii, 482.

⁶ de Havilland Hall. *Lancet*, Lond., 1902, i, 593; *Trans. Med. Soc. Lond.*, 1902, xxv, 191.

⁷ Courvoisier. *Path. u. Chir. d. Gallenwege*, 1890.

In nearly all cases recovery takes place from the actual attack, but it is seldom that the first attack is the last. Usually there are further and less severe bouts. After a series of these attacks the patients may be free from any further trouble. But a calculus is sometimes left in the common bile-duct and the symptoms of intermittent hepatic fever develop, or there is constantly recurring pain from adhesions around the gall-bladder (*vide* p. 758). The prognosis in some degree depends on the presence or absence of facets on a calculus found in the stools. If, after a first attack, a smooth gall-stone without facets is found in the faeces, it may reasonably be hoped that no further attacks will follow. If, on the other hand, the calculus is faceted, there are more calculi in the gall-bladder and the probability of fresh attacks must be faced. The patient's habit of life, his willingness or refusal to avoid conditions which favour catarrhal cholecystitis and the production of fresh gall-stones, bear on the prognosis.

Treatment.—The pain is often so agonising that it will yield to nothing except hypodermic injections of morphine or inhalations of chloroform. After a hypodermic injection has been given, a few whiffs of chloroform will relieve the pain until the effect of the morphine makes the patient comfortable. One-fourth to a half of a grain of morphine combined with $\frac{1}{100}$ grain of atropine may be injected in these cases, and if an inhalation of chloroform is not advisable, 20 minims of chloroform in water may be given by the mouth (Gilman Thompson¹). A hypodermic injection of morphine is very much better than opium by the mouth, both because it acts more rapidly and because repeated vomiting may lead to rejection of everything taken by the mouth. The hypodermic syringe should, of course, never be entrusted to the patient.

A graphic account of the intense suffering involved in breaking off the morphine habit acquired from repeated biliary colic is given by Keay in his book on the *Medical Treatment of Gall-stones*, p. 105.

The vomiting accompanying the biliary colic hardly requires any special treatment apart from that of the pain, as it will cease with it. Bismuth, soda, dilute hydrocyanic acid, and iced apollinaris or soda-water may be given. Large draughts of water containing bicarbonate of sodium (3j to Oj), recommended by Prout, relieve purposeless retching by giving the stomach something to bring up. If retching persists and the patient be collapsed, iced champagne may be tried; otherwise it is better to give nothing by the mouth, to apply poultices to the epigastrium, and to keep the patient under the influence of morphine.

In less severe cases the patient may be put in a hot bath (104° F.) and given tincture of belladonna (℥xx.) in spirits of chloroform to relieve spasm, or the following draught: Turpentine (℥xv.), spiritus aetheris (℥xxx.), aquam chloroformi to the ounce. Antipyrin, if given at the beginning of an attack, has been thought to give relief, but Kraus² considers that it

¹ Gilman Thompson. *Med. News*, N.Y., 1897, lxx, 516.

² Kraus. *On Gall-stones*. p. 83. English transl., 1896.

Symptoms suggesting recurrence such as
 colic, pain, jaundice occur in from 2 to
 10 p.c. of ~~some~~ cases (Stanton; Judd) and
 may be due to calculi overlooked at operation
 to ^{their} new formation, or to post-operative stricture of the common duct
 (Judd and Burdett)

among 2029 gall bladder
 operations reported 219 or
 10.8 p.c. requiring further
 operation

which Stanton estimates
 as occurring in from 2
 to 10 per cent;

Stanton, however, states that the
 reported cases do not bear out
 the assumption that cholecystectomy
 affords a greater immunity than
 cholecystotomy; and at the present
 time removal of the gall bladder
 is the ~~more~~ ^{more} accepted course

Stanton. Ann. Surg., 1915, Lxi, 226
 Judd. Ann. Surg., 1916, Lxviii, 472
 Judd and Burdett. Ann. Surg., 1922,
 Lxx, 216

does good chiefly by inducing profuse perspiration, and insists on its futility when the attack has lasted two to three hours. Robson¹ recommends aspirin 5–10 grs., and exalgin in 1 gr. doses every half-hour for three or four doses. Naunyn² has had favourable results with a single dose of salicylate of sodium (30–45 grains) given at the beginning of an attack. Some observers recommend several ounces of olive oil; possibly relief of pain may be due to the oil inhibiting the secretion of HCl in cases with hyperchlorhydria. Washing out the stomach has been thought to alleviate the pain (Baruch³). Hot fomentations or poultices may be tried over the liver.

The external application of salicylate of methyl over the liver has been recommended in hepatic colic: 1 to 2 drams may be painted on daily and covered with gutta-percha to favour absorption. Chambart-Hénon⁴ says it gives relief in half an hour.

Surgical Treatment.—During an attack of biliary colic operation is justified only in the presence of severe complications which would otherwise prove fatal. These complications are (i) rupture of the gall-bladder or bile-ducts, with severe collapse and signs of perforative peritonitis; (ii) widespread peritonitis due to acute infective inflammation of the gall-bladder, and (iii) signs of acute intestinal obstruction due to volvulus of the intestine from exaggerated peristalsis.

When, in spite of medical treatment, attacks of colic continually recur and the patient becomes incapacitated and is in danger of contracting the morphine habit, surgical measures must be considered. The gall-bladder should be opened, calculi removed, and, if necessary, the gall-bladder excised. Some difference of opinion has, perhaps naturally, existed between physicians and surgeons as to the recurrence of cholelithiasis after the operative removal of calculi from the gall-bladder. *cholecystotomy* Reference has been made on p. 744 to 8 cases in which fresh calculi formed around sutures introduced into the wall of the gall-bladder during an operation for the removal of calculi. On the other hand, recurrence is very rare; for in 1500 operations on the gall-bladder and bile-ducts gall-stones re-formed in the gall-bladder in one case only (Mayo⁵). Many supposed examples of recurrence are due to incomplete removal of calculi from the ducts.

It might appear that when operation is required in recurrent biliary colic, the gall-bladder should either be removed or so treated that no fresh formation of gall-stones in it is possible. *unless it is healthy.* Mayo, however, considers that cholecystectomy should not be done as a routine course, because it is not necessary from the point of view of recurrence and because it renders subsequent drainage or cholecyst-enterostomy impossible. The treatment during the intervals is the general treatment of cholelithiasis described on page 744.

¹ Robson. *System of Medicine* (Allbutt and Rolleston), 1908, iv, part i, 263.

² Naunyn. *Cholelithiasis*, p. 178. Transl. New Sydenham Soc., 1896.

³ Baruch. *Principles and Practice of Hydrotherapy*, p. 235, 1900, Lond.

⁴ Chambart-Hénon. *Gaz. méd. de Paris*, 1898, 11. s., i, 408.

⁵ Mayo. *Ann. Surg.*, 1906, xlv, 209.

III. THE MECHANICAL EFFECTS OF GALL-STONES will be considered under the following heads, according as the stones are: (1) in the gall-bladder; (2) in the cystic duct; (3) in the common bile-duct; (4) in the ampulla of Vater; and (5) intestinal obstruction.

(1) **Mechanical Effects of Gall-stones in the Gall-bladder.**—The mechanical effects pure and simple of calculi in the gall-bladder are not very frequent, or, as a rule, very important. A large calculous gall-bladder may give rise to a feeling of dragging or heaviness and discomfort in the region of the liver. ~~The~~ gall-bladder, ~~when~~ full of tightly packed calculi or containing a large single gall-stone, may press on the pylorus or duodenum, and by producing pyloric obstruction and dilatation of the stomach, may imitate carcinoma of the pylorus (Naunyn,¹ Potherat²). In these cases examination of the gastric contents may be of use in settling the diagnosis: free hydrochloric acid should be present in cholelithiasis, whereas in gastric carcinoma it should be absent; but I have seen gall-stones in the gall-bladder necessitate operation in a case of carcinoma of the stomach with a normal amount of HCl in the gastric juice. Unless the calculi contain lime salts no shadow is thrown by x-rays. Gall-stones in the gall-bladder do not, as a rule, obstruct the outflow of food from the stomach simply and solely in a mechanical way, but set up spasm or adhesions between the pylorus and the gall-bladder which contract and slowly lead to pyloric obstruction (*vide* p. 758). A large single calculus ulcerating out of the gall-bladder into the duodenum may mechanically obstruct the pylorus (*vide* p. 769). There may be a combination of cholecysto-gastric fistula, adhesions around the pylorus, and mechanical obstruction of the lumen of the pylorus by a calculus.

From the pressure of a large calculous gall-bladder the common bile-duct might be compressed and jaundice set up. Thrombosis of the portal vein from this cause has been reported.³ From traction exerted by a gall-bladder containing calculi the right lobe of the liver may be elongated into a Riedel's lobe. Axial rotation of a long cystic duct of a calculous gall-bladder has been observed (Wendel⁴).

The gall-bladder filled with calculi may be felt as a hard tumour through the abdominal wall, sometimes just below the costal arch; in other cases, owing to the presence of a Riedel's lobe, the gall-bladder is considerably depressed and may be found in the neighbourhood of the right iliac fossa. Unless fixed by adhesions, the calculous gall-bladder moves with respiration and can be displaced in a lateral direction. When there are numerous calculi, crepitus may be detected on palpation over the tumour, but this is often absent.

When the gall-bladder is filled with gall-stones and its walls are much atrophied, spontaneous rupture may possibly occur; but in most cases ulceration and softening due to inflammation are responsible for

¹ Naunyn. *On Cholelithiasis*, p. 151. Transl. New Sydenham Soc., 1896.

² Potherat. *Bull. et mém. Soc. de chir.*, Paris, 1903, n.s., xxix, 669.

³ Donkin. *Med. Times and Gaz.*, 1868, ii, 396.

⁴ Wendel. *Ann. Surg.*, 1898, xxvii, 199.

Gosset. Rev. de chir., Par., 1912, XLVI, 964.

The epithelium may disappear; and
the "white bile" is devoid of bile
salts or pigment, being an exudate
from the blood vessels (Gooset, Loewy
and Meotregat)

Gooset, Loewy et Meotregat, Procc. med., Par., 1921, XXIV,
192

rupture of a gall-bladder containing calculi (*vide* p. 773). The presence of calculi in the gall-bladder disposes to primary carcinoma; this is discussed elsewhere (*vide* p. 638).

(2) **Mechanical Effects of Calculi in the Cystic Duct.**—When a calculus passes into the cystic duct, it stretches the walls and sets up spasm and biliary colic (*vide* p. 731). A calculus may remain impacted in the cystic duct for long periods; sometimes no definite history of past colic is forthcoming in such cases to mark the time of impaction. The calculus is nearly always fixed ~~close to~~ ^{in Hartmann's} to the neck of the gall-bladder. It may completely obstruct the flow of bile into the gall-bladder, which then becomes distended with mucus, at first mixed with bile, but later quite clear. Its walls may become extremely thin, or may be thickened from inflammation. ^{pouch at} This is hydrops vesicae felleae, or mucocele of the gall-bladder. Infection and cholecystitis are very prone to occur under these ^{obstructive} conditions. The distended gall-bladder may be the site of painful spasmodic contractions resembling biliary colic, except that jaundice is usually absent; in these cases the condition is very likely to be regarded as indigestion. Nausea and persistent vomiting may be very troublesome. I have seen fatal vomiting in a woman in whom the presence of small calculi in the cystic duct was the only morbid condition at the necropsy. Jaundice may, however, be brought about by extension of spasm to, or by concomitant inflammation of, the common bile-duct. According to Riedel,¹ jaundice is present in from 10 to 15 per cent of the cases in which a calculus is impacted at the neck of the gall-bladder. Attacks of painful spasm with intermittent distension of the gall-bladder have been explained as depending on the valvular action of a calculus in the neck of the gall-bladder which allows bile to enter the gall-bladder but not to leave it. It is, however, more probable that the distension of the gall-bladder is due to inflammation of the mucosa of the cystic duct, which also accounts for some of the pain. Conversely it has been stated that the valvular action of the calculus may only allow mucus to pass out of the gall-bladder.

A *distended gall-bladder* appears as an abdominal tumour in the right half of the abdomen; in very rare instances it is so large as to occupy the greater part of the abdomen, and has been mistaken for ascites and tapped.

In a case of Lawson Tait's² it contained 11, in Collinson's³ 25, and in Terrier's⁴ 42 pints of fluid. Large cystic gall-bladders occur almost always in women.

Usually it is not larger than the closed fist; it is pear-shaped at first, and as it grows becomes cucumber-shaped (Doran⁵). The dilated gall-bladder may be associated with a Riedel's linguiform lobe, and as a result

¹ Riedel. *Berlin. klin. Wchnschr.*, 1901, xxxviii, 78.

² Tait, L. *Lancet*, Lond., 1889, i, 1294.

³ Collinson. *Brit. Med. Journ.*, 1909, i, 1294.

⁴ Terrier. *Bull. Acad. de méd.*, Paris, 1890, 3. s., xxiv, 831.

⁵ Doran. *Brit. Med. Journ.*, 1905, i, 1316.

the gall-bladder may form a tumour in the right iliac fossa and imitate appendicitis. H. J. Waring¹ figures a gall-bladder which entered into a right femoral hernia. It forms a smooth, tense, pear-shaped tumour with the apex upwards and the base downwards. It usually moves with respiration and can be displaced laterally, but not downwards. It is separated from the liver by a groove or depression, is immediately under the abdominal walls, and in thin patients may be visible as a raised surface. It is not tender unless there is concomitant inflammation. It may be resonant on percussion. A gall-bladder distended with mucus from obstruction of the cystic duct may subsequently shrivel up.



FIG. 106.—Calculus impacted in the cystic duct; cholecystitis with distension of the gall-bladder, mucocele. St. George's Hospital Museum. Series ix, 199g.

A distended gall-bladder must be distinguished from a floating kidney, a renal tumour or hydronephrosis, a tumour of the pylorus, a growth in the transverse colon, an ovarian cyst fixed by adhesions. Confusion is most likely to arise between a distended gall-bladder and a floating kidney on the right side, since both are commoner in women and may be accompanied by attacks of severe pain followed by jaundice. An enlarged gall-bladder forms a tumour which is much more constant and does not disappear or vary in position in the same way as a floating kidney. A gall-bladder is usually movable, but is limited by its attachment to the liver and cannot be displaced into the false pelvis like a floating kidney. If displaced backwards towards the loin, it returns to its former position directly the pressure is removed,

whereas a floating kidney tends to remain there as long as the patient is recumbent. A distended gall-bladder does not escape from one's grasp in the same way that a floating kidney does. A careful bimanual examination should always be made. Distension of the colon with air (Ziemssen's test) may be useful, as it should press the gall-bladder forwards and displace a floating kidney backwards; but it is not infallible. Mayo Robson met with a case in which it pushed a growth of the right supra-renal forwards. Kehr also distrusts this test, as the colon may pass in front of the gall-bladder. In a fat person it may be very difficult to distinguish between a floating kidney and a distended gall-bladder. ~~In~~ In some cases a floating kidney and a distended gall-bladder may both be present, and may be adherent to each other (Reymond²).

¹ Waring. *Diseases of the Liver*, p. 235, 1897.

² Reymond. *Rev. de chir.*, Paris, 1900, xxi, 749.



Chance¹ described a dilated gall-bladder containing 200 calculi which exactly imitated a tuberculous kidney.

A tumour of the pylorus lies in a plane, roughly speaking, at right angles to that of the gall-bladder and is hard and tender. In gall-bladder cases there may be gastric symptoms and some dilatation of the stomach from pyloric obstruction, but the gastric symptoms are not so prominent as in pyloric new-growth. A tumour of the transverse colon is less sharply defined than a dilated gall-bladder, and, like the pyloric tumour, tends to have its long axis at right angles to that of a distended gall-bladder. Faecal impaction in the transverse colon will usually be accompanied by faecal masses elsewhere in the abdomen, and the condition will be cleared up or altered by the use of enemas. It may be impossible to distinguish between a small dependent hydatid cyst and a dilated gall-bladder until the abdomen is opened (*vide* p. 628). Aspiration would settle the matter, but this is too dangerous a method to be recommended.

In a woman aged forty a dilated gall-bladder containing 11 pints of liquid, due to a calculus impacted in the cystic duct, imitated a parovarian cyst (L. Tait²).

Naunyn³ quotes two cases in which a calculus in the cystic duct exerted direct pressure—on the portal vein in one instance, and on one of its branches in the other—and set up pylethrombosis. Haematemeses may thus be an indirect result of cholelithiasis. A calculus in the cystic duct may possibly exert pressure on the common hepatic duct and so give rise to jaundice.

The passage of calculi along the cystic duct dilates and straightens out the tortuous lumen of the duct, and so facilitates the subsequent passage of calculi from the gall-bladder. The valves of Heister, which under ordinary conditions obstruct the return of a calculus from the duct into the gall-bladder, become almost obliterated and only appear as slight elevations of the mucous membrane; when thus altered, they may allow a calculus to travel towards the gall-bladder.

In a case under my care a large gall-stone in the common duct was displaced at a laparotomy, undertaken for its removal, by manipulation, and was thought to have passed into the duodenum. At the necropsy, however, it was in the gall-bladder (*vide* p. 558).

(3) **Mechanical Effects of Gall-stones in the Common Bile-duct.**—The passage of a calculus through the common bile-duct sets up biliary colic (*vide* p. 731). A calculus may, however, pass into the common duct and become permanently lodged there without giving rise to the symptoms of colic. While in the common duct the calculus increases in size from deposit on its outer surface.

¹ Chance. *Med. Chron.*, Manchester, 1902, xxxvii, 120.

² Tait. *Lancet*, Lond., 1889, i, 1294.

³ Naunyn. *Cholelithiasis*, p. 123. Transl. New Sydenham Soc., 1896.

Situation of the Calculi in the Common Duct.—Though statistics are not unanimous, the commonest site for calculi appears to be the lower end of the common duct and the ampulla Vateri.

In Courvoisier's 123 cases the calculi were found to occupy the whole of the common bile-duct in 26 ; the upper segment in 17 ; the middle segment in 19 ; to be close to the duodenum in 20 ; in the orifice of the biliary papilla in 41 ; so that in almost exactly half the cases the calculus was close to the lower end of the duct. In 380 operation cases Mayo Robson¹ found the calculus in the duodenal end in 67 per cent ; in the middle portion in 18 per cent ; and at the upper end in 15 per cent. From a smaller number of cases Vautrin² came to the opposite conclusion : number of cases, 47 ; calculi in part of the duct above the duodenum, 27 ; in part of duct in contact with the duodenum, 18 ; in the ampulla Vateri, 2. This distribution he explained by the fact that the duct is readily dilatable above the duodenum, but resists dilatation where it is supported by the pancreas. The passage of a calculus from the lower end of the common duct into the ampulla is probably a matter of time.

Number of Calculi in the Common Duct.—In the great majority of cases there is a single calculus ; thus, in 149 observations Courvoisier³ found that in 95 there was a single calculus, in 36 instances there were from two to six calculi, and in the remaining 18 a dozen or more calculi in the duct. A single calculus is usually firm, but there may be a soft, crumbling mass which fills the whole of the dilated duct and may extend into the common hepatic duct. Several soft crumbling calculi may be found. Mayo Robson once removed 88 calculi from the common duct.

Results and Clinical Features.—A calculus in the common duct often sets up inflammation, the manifestations of which are fully described on p. 759. Here we are only concerned with the purely mechanical effects. Reflex irritation of calculi in the common duct may give rise to vomiting. Leclerc⁴ reports a case in which vomiting persisted for forty days until two calculi were removed from the common duct ; there was no other cause, such as adhesions or pyloric obstruction, for the vomiting.

A calculus may completely obstruct the common duct, partially occlude the lumen so that some bile can run past it into the duodenum, or be floating in the common duct and exert a ball-valve action (Osler,⁵ Fenger⁶). A calculus which at first is firmly impacted and completely occludes the common duct may subsequently become loose. This is due to several factors ; the obstruction dilates the ducts above and thus leads to widening of the duct at the point of impaction ; the constant pressure of the calculus produces atrophy of the walls of the common duct, while inflammatory softening and ulceration are extremely likely to occur. It

¹ Mayo Robson. *Diseases of the Gall-bladder and Bile-ducts*, p. 278, 1904.

² Vautrin. *Rev. de chir.*, Paris, 1896, xvi, 454.

³ Courvoisier. *Path. u. Chir. d. Gallenwege*, 1890.

⁴ Leclerc. *Lyon méd.*, 1903, c, 737.

⁵ Osler, W. *Med. Times and Gaz.*, 1881, ii, 111.

⁶ Fenger, C. *Am. Journ. Med. Sc.*, Phila., 1896, cxi, 125.

i Oertel records such a
Case in which there must
have been complete
obstruction | ^

OERTEL, H. Arch. Int. Med., Chicago, 1918, XXI, 7

is, therefore, rare for absolute biliary obstruction to persist for a long time, but jaundice may be kept up both by intermittent obstruction depending on the ball-valve action of a calculus and also by concomitant inflammation of the bile-ducts (*vide* p. 759). Jaundice which has been marked early in the course of the impaction may wane and finally disappear, and after death a loose calculus may be found in the duct. Griffon¹ records four cases of this kind in which the calculus was found just above the biliary papilla. In exceptional instances there may never at any time be jaundice although the common duct contains calculi;^

Chronic obstruction of the bile-duct with calculi may, however, induce long-standing jaundice. In these cases there may be a large crumbling calculous mass occupying a considerable extent of the common bile-duct. A calculous accumulation of this kind grows from deposit of bilirubin-calcium and is accompanied by infective cholangitis. When the duct contains a single calculus, jaundice, though present for a time, usually passes away. The occurrence of malignant disease of the duct at the site of a calculus is very rare.

As the result of obstruction of the common duct by calculi there may be (i) cylindrical or (ii) saccular dilatation of the duct. (i) *Cylindrical dilatation* is the commoner. The duct is often the size of a chemical test-tube, and may be larger and resemble a piece of intestine. The cylindrical dilatation may spread through the common and hepatic ducts into the intrahepatic bile-ducts. The dilatation is more marked on the surface of the organ, and is often more prominent in the left lobe, probably because there is less resistance on the surface of the liver and especially in the smaller left lobe. Local saccular dilatation of the varicose bile-ducts on the surface of the liver may occur.

(ii) *Saccular Dilatation*.—In rare instances the common bile-duct may form a large cyst which may be diagnosed as a dilated gall-bladder, a pancreatic cyst, a hydatid cyst, etc. The condition is like that described on p. 659. Occasionally there are local cystic dilatations in the intrahepatic branches of the bile-ducts on the surface of the liver; this local dilatation may be superimposed on a widespread cylindrical dilatation.

Simply from distension with bile *the liver* becomes at first enlarged. Subsequently atrophy of the liver cells occurs, with prominence of the existing fibrous tissue. The question whether mere stasis of the bile can lead to genuine hepatic cirrhosis has given rise to considerable discussion and experimental investigation (*vide* p. 327). The conclusions from human morbid anatomy are that biliary obstruction alone does not induce real cirrhosis, but if infection of the bile-ducts occurs, pericholangitic fibrosis will result. In obstruction of the ducts with calculi infective cholangitis is readily produced, and thus fibrosis of the liver may result.

In very rare instances a calculus in the common bile-duct may

¹ Griffon. *Bull. Soc. Anat. Paris*, 1896, lxxi, 513.

mechanically compress the portal vein and give rise to thrombosis (Naunyn,¹ Westenhoffer,² Körte³).

Diagnosis.—In cases in which a stone has entered the common duct without any symptoms of colic, the painless and gradual onset of jaundice may suggest carcinoma of the head of the pancreas. The differential diagnosis is considered on p. 762.

(4) **The Mechanical Effects of a Calculus in the Ampulla of Vater.**
—A calculus may bulge the papilla into the duodenum, and prolapse of the terminal portion of the duct comparable to prolapse of the ureter into the urinary bladder has been described (Bland-Sutton⁴). A difference between the mechanical effects of a calculus in the ampulla and of one in the lower end of the bile-duct is that a calculus in the ampulla of Vater may in addition obstruct Wirsung's duct. The accessory duct of Santorini may, however, carry off the secretion into the duodenum, and so prevent any accumulation of the pancreatic juice in the ducts. In about one-third of the cases, however, there is no communication between the two ducts (Schirmer⁵), and in these cases obstruction of the orifice of Wirsung's duct would lead to its distension with pancreatic secretion.

As a matter of fact, however, there is nearly always some additional inflammatory change when a calculus is in the ampulla of Vater. This sets up pancreatitis and leads to enlargement and fibrosis of the pancreas, dilatation of Wirsung's duct, and in some instances to the formation of pancreatic calculi. The chronic interstitial pancreatitis due to obstruction of the ducts is hardly ever so extensive as to destroy the islands of Langerhans, or to cause glycosuria or diabetes (Opie⁶).

When a small calculus is impacted in the ampulla of Vater close to the biliary papilla and is not sufficiently large to obstruct the opening of the main duct of the pancreas into the ampulla Vateri, the direct mechanical obstruction to the flow of bile into the duodenum results in the passage of bile into the pancreatic duct. This has been shewn by Halsted and Opie⁷ and by Bunting⁸ to have occurred in fatal hæmorrhagic pancreatitis. Opie, moreover, proved by experiments on dogs that the passage of bile into the pancreatic duct induces hæmorrhagic pancreatitis; and Flexner⁹ has shewn that the bile salts are the active factor in producing pancreatitis, whilst the colloid constituents of the bile exert a protective action. He suggests that bile containing a large amount of mucilaginous (or colloidal) constituents, as in biliary obstruction, or of albuminous products, as in inflammatory conditions, provides exactly the theoretical requirements for subacute or chronic lesions of the pancreas,

¹ Naunyn. *Cholelithiasis*, p. 133. Transl. New Sydenham Soc., 1896.

² Westenhoffer. *Semaine méd.*, Paris, 1903, xxiii, 33.

³ Körte. *Ibid.*

⁴ Bland-Sutton. *Gall-stones and Diseases of the Bile-ducts*, p. 87, 1907.

⁵ Schirmer. *Inaug. Dissert.*, Basel. Quoted by Opie. *Am. Journ. Med. Sc.*, Phila., 1901, cxxi, 30.

⁶ Opie, E. L. *Journ. Exper. Med.*, N.Y., 1901, v, 397.

⁷ Halsted and Opie. *Johns Hopkins Hosp. Bull.*, Balt., 1901, xii, 179.

⁸ Bunting. *Ibid.*, 1906, xvii, 265.

⁹ Flexner. *Journ. Exper. Med.*, N.Y., 1906, viii, 167.

Archibald on experimental
grounds argues that spasm of
Oddi's Sphincter causes
retrojection of infected bile
into the pancreatic duct.

Acute pancreatitis, especially when
haemorrhagic, causes severe shock, and
pain in the back. Glycosuria is
inconstant. The diastase index
of the urine may be much raised;
Loewi's test should be tried.

Wagner in 1914

Index written in

Wagner Ztschr. f. klin. Chir. 1914, cxxx.

Archibald, B. Surg., Gyn., & Obstet.,
1919, xxviii,
529.

should such bile enter the pancreatic duct. The reason why impacted calculi in the ampulla of Vater only rarely induce haemorrhagic pancreatitis is that usually the calculi are sufficiently large to obstruct the orifice of Wirsung's duct and to interfere with the entrance of bile into the pancreatic duct. Williams and Busch,¹ however, suggest that the passage of gall-stones may so dilate the opening of papilla that intestinal contents are able to pass into the pancreatic duct and produce inflammation and necrosis of the pancreas. A pancreatic calculus which passes into the ampulla of Vater would differ from a gall-stone in giving a shadow with x-rays and causing distension of the gall-bladder (Murray²).

(5) Mechanical Obstruction of the Intestines by Gall-stones.—

Incidence.—When a large gall-stone ulcerates out of the gall-bladder into the duodenum, or in rare instances into the colon, it may produce mechanical obstruction of the bowel. This is decidedly rare; thus at the Leeds Infirmary, where a large number of gall-stone operations are done, only one case occurred in ten years,³ and there were three cases at St. George's Hospital in twenty-one years. But from the interest attaching to such rare and striking cases a large number have been reported, and Morestin,⁴ in 1900, was able to refer to as many as 242 cases. The relative frequency of this cause to other causes of intestinal obstruction has been variously estimated at from 1 to 13 to 1 to 45.

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In 295 cases of intestinal obstruction Fitz found 23 due to gall-stones, or 1 in 13; Gibson,⁵ 40 in 696, or 1 in 17; Leichtenstein, 41 in 1152, or 1 in 28; in 669 consecutive cases of intestinal obstruction in thirteen years at the London Hospital, Barnard⁶ found 15, or 1 in 45, due to gall-stones.

Entrance of the Calculus into the Intestine.—It is probably very seldom that a calculus which passes down the bile-duct into the duodenum is of sufficient size to occlude mechanically the ileo-caecal valve. In some instances a large calculus is found projecting from the lower end of the bile-duct, and it is conceivable that such a calculus, after squeezing through the biliary papilla into the duodenum, would be large enough to obstruct the ileo-caecal valve. It is probable that a comparatively small calculus, after passing into the intestine, may increase in size from addition of phosphates to its surface, as in Eve's case,⁷ and so become large enough to obstruct the ileum or ileo-caecal valve. Treves⁸ removed a calculus, with a diameter in its long axis of $1\frac{1}{2}$ inches, from the ileum of an old lady who for years had taken carbonate of magnesium daily. Its nucleus was a small gall-stone, and its large size was due to layers of magnesia and faecal material. In very rare instances intestinal

¹ Williams and Busch. *Journ. Med. Research*, Boston, 1907, xvii, 35.

² Murray. *Proc. Roy. Soc. Med.*, 1912, v (Surg. Sect.), 131.

³ Vide Moynihan. *Med. Chron.*, Manchester, 1903, xxxviii, 277.

⁴ Morestin. *Bull. Soc. Anat. Paris*, 1900, lxxv, 196.

⁵ Gibson, C. L. *Ann. Surg.*, 1900, xxxii, 506.

⁶ Barnard, H. L. *System of Medicine* (Allbutt and Rolleston), 1907, iii, 744.

⁷ Eve, F. *Trans. Clin. Soc.*, Lond., 1895, xxviii, 91.

⁸ Treves, F. *Intestinal Obstruction*. p. 193, 2nd ed., 1899.

obstruction may be due to impaction of a congeries of small calculi in the intestine (Cantlie¹). A calculus not sufficiently large to obstruct the normal small intestine may, if the intestine is narrowed from some other cause, completely obstruct the stricture.

Thus Mayo Robson² found a calculus entangled in a pouch between two tuberculous strictures of the ileum. Garrett³ found a gall-stone arrested where the small intestine passed under an omental cord; the bowel was thus completely occluded. Moynihan⁴ found a large gall-stone fitted as tightly as a cork in the lumen of a malignant mass at the ileo-caecal valve. Bush⁵ found a gall-stone completely occluding the intestine in a hernial sac.

A comparatively small calculus may, especially if it is angular, set up spasm of the intestinal wall around the calculus, and so lead to closure of the lumen of the bowel; this explains why in some fatal cases of gall-stone obstruction the calculus has been found loose in the bowel. Another method by which a comparatively small calculus may cause intestinal obstruction is by setting up localised inflammation of the mucous membrane of the bowel in its immediate neighbourhood. The resulting swelling and spasm of the wall of the bowel may then lead to impaction of the calculus.

In the vast majority of cases mechanical obstruction of the intestine by gall-stones is due to a large calculus which has ulcerated out of the gall-bladder into the duodenum, or less commonly into the transverse colon. Intestinal obstruction is much more likely to follow the passage of a calculus into the duodenum, as it has then to pass through the jejunum and the narrowed lower part of the ileum, than in cases in which a calculus ulcerates directly from the gall-bladder into the colon.

It is stated that a calculus may enter the intestine and remain there comparatively quietly for days, months, or even years, and yet eventually give rise to intestinal obstruction. Ulceration and thickening of the lower part of the ileum have been found in association with a number of calculi in that position (N. Ward⁶). When a calculus is in the intestine, it may set up repeated attacks of colic, vomiting, and pain, suggesting mild obstruction, and finally bring about acute obstruction.

In Anderson and Smith's⁷ case the calculus was thought to have entered the intestine fifteen and in Eve's case ten years before acute obstruction was produced.

As there may be two calculi in the intestine, attacks of transient obstruction may recur even after a calculus has been passed by the bowel.

It is probable that all large calculi spontaneously passed by the bowel

¹ Cantlie, J. *Brit. Med. Journ.*, 1904, i, 181.

² Mayo Robson. *Trans. Clin. Soc.*, Lond., 1902, xxxv, 58.

³ Garrett. *Brit. Med. Journ.*, 1902, ii, 789.

⁴ Moynihan. *Clin. Journ.*, Lond., 1906-7, xxix, 411.

⁵ Bush. *Bristol Med.-Chir. Journ.*, 1903, xxi, 301.

⁶ Ward, N. *Trans. Path. Soc.*, Lond., 1850-52, iii, 365.

⁷ Anderson and Smith. *Lancet*, 1887, ii, 1103.

← In Drew's case the distended bowel showed few gas cysts in its wall

In Péraire's case symptoms of obstruction recurred
some days after a calculus had been removed by
enterotomy, but recovery followed spontaneous
evacuation of a second calculus.

Small
print

Péraire. Bull. Soc. anat., Par., 1913, 6. s., xv, 355

Drew, D. Brit. Journ. Surg., Bristol, 1925, xii, 803



have entered the transverse colon from the gall-bladder by a cholecystocolic fistula, for a calculus with a diameter of an inch or more would almost certainly become impacted at the ileo-caecal valve. Among Gibson's¹ 40 cases the largest gall-stone weighed three and a half ounces.

Site of the Obstruction.—The obstruction is most frequent in the lower end of the ileum near the ileo-caecal valve. When a large calculus ulcerates from the gall-bladder into the duodenum, the site of the obstruction may be in the duodenum itself, at its junction with the jejunum, or in the ileum. When a calculus ulcerates into the colon, the obstruction may occur in the sigmoid flexure or close to the anus. As seen at operation the contraction of the empty intestine immediately below the calculus produces a septum on which the calculus rests (Barnard).

In 104 cases Lesk² found the site of obstruction to be in the duodenum in 5, in the jejunum in 17, in the ileum in 36, in the ileum near the ileo-caecal valve in 26, in the small intestine (not further specified) in 13, in the colon in 6, and in the rectum in 1. In 40 cases collected by Gibson the calculus was impacted in the large intestine in one case only; in the ileo-caecal valve in one instance, and in all the other cases in the small intestine. The larger the gall-stone, the higher up in the small intestine will it be arrested (Barnard).

Sex.—Intestinal obstruction due to gall-stones is very much commoner in women than in men. This is a natural result of the great frequency of cholelithiasis in women. 1) 11

In Lesk's 148 cases 39 were men and 109 women. In 50 cases which I have collected there were 42 females and 8 males.

The average age is over 50 years of age. In 50 recent cases the average age was 62·7 years, and many cases between 70 and 80 years of age have been reported. In Lesk's 148 patients there were 6 under 40 years of age.

Clinical Picture.—The onset is sudden. In some cases it has been preceded by attacks of vomiting and pain, but usually signs suggesting that the calculus has been for some time in the bowel are absent, and there may be no evidence of former gall-bladder trouble or of cholelithiasis. In 41 out of 120 cases the onset was preceded by symptoms which could be referred to ulceration of the calculus into the intestine (Naunyn). Although the bowel is obstructed, it is not strangulated, and as the circulation through its walls is not interfered with, they do not become paralysed and hence tympanites is usually absent, and flatus and faeces are often passed by the bowel. A calculus has been known to ulcerate out of the bowel and set up peritonitis.³ At first pain and collapse are not marked. When the calculus is entering the duodenum the pain is referred to the epigastrium, later when it has passed into the

¹ Gibson. *Ann. Surg.*, 1900, xxxii, 506.

² Lesk. *Deutsche Ztschr. f. Chir.*, Leipz., 1908, xcix, 47.

³ Jeaffreson. *Brit. Med. Journ.*, 1868, i, 531.

small intestine the pain is more diffuse and referred to the umbilicus. Vomiting is an early symptom and extremely profuse, and when the calculus is impacted in the duodenum or in the upper part of the small intestine, the vomited matter is bilious and may become stercoraceous. It may contain blood from haemorrhage produced in the ulceration of the calculus into the duodenum.

As the calculus passes down the small intestine the vomiting becomes less copious; this remission usually occurs on the third day (Barnard). After this the calculus may become impacted, so that unless relieved by operation death occurs from acute obstruction. In about 50 per cent the symptoms are spontaneously relieved, sometimes quite suddenly, so that the patient at once knows that his condition has improved. In some instances, even though the patient has been relieved from the acute symptoms of obstruction, the wall of the bowel is so damaged that perforation or leakage from an ulcer occurs and sets up peritonitis.

Duration and Prognosis.—In fatal cases death from collapse usually occurs within five to ten days after the onset. In Sands' case¹ recovery took place after the condition had lasted for twenty-eight days; this is the longest case on record. About 50 per cent of the cases die if not operated upon. The statistics of cases operated upon shew a high mortality; thus, in Schüller's 82 cases 56 per cent, in Sir J. Hutchinson's 50 per cent, and in Courvoisier's 125 cases of operation, 44 per cent, died. The advanced age of the patients is, no doubt, partly responsible for this high mortality; but operation after the fourth day of obstruction is hardly ever followed by recovery (Barnard).

Diagnosis.—When there is a definite history of gall-stones in the past and acute obstruction comes on suddenly with the disappearance of a tumour in the position of the gall-bladder, and the presence of a hard lump elsewhere in the abdomen, the diagnosis would appear to be fairly clear. But, unfortunately, in a number of the cases there is no history of cholelithiasis, and the gall-stone is hardly ever felt in the abdomen before the operation. In two cases reported by Barnard² the calculus was felt before operation. It is possible that examination under an anaesthetic *Sometimes* might enable a calculus to be felt ~~in a certain number of cases.~~ But as a matter of fact, the condition is very seldom correctly diagnosed before the abdomen is opened or the calculus is spontaneously passed by the rectum.

Treatment.—As the symptoms are those of intestinal obstruction and it is seldom possible to make a certain diagnosis of mechanical obstruction due to a gall-stone, the safest course is to open the abdomen and remove the stone by incising the bowel. In cases in which the stone is comparatively small and is impacted at the lower end of the ileum, it might be pressed on into the colon. It is important that if an operation is necessary, it should be undertaken as soon as possible, for the patients are usually elderly and are often wanting in vitality.

¹ Quoted by Treves. *Intestinal Obstruction*, p. 388, 2nd ed., 1899.

² Barnard, H. L. *Ann. Surg.*, 1902, xxxvi, 161.

In Neligan's case 30 faceted gall stones were vomited.

Out of Wagner's 334 collected cases
161 were operated upon with 62 per
cent. mortality, and 173 were not
operated upon and 46 per cent.
proved fatal.

NELIGAN, R.A. Lancet, 1915, 1, 1023.

Wagner. Deutsches Ztschr. f. Chir., 1914, cxxx, 353

Medical treatment has been successful in a certain number of cases. The most reasonable method seems to be to give belladonna or atropine in order to relieve spasm, and so to allow of the onward passage of the calculus; this method should be adopted in less severe cases in which there is any reason to suspect or believe that the cause of obstruction is an impacted calculus in the intestine, and at an early stage. In such cases Mayo Robson¹ advises morphine to relieve the pain, and extract of belladonna ($\frac{1}{4}$ gr.) every four hours. Under chloroform anaesthesia a thorough examination of the abdomen can be made, by which the diagnosis may be cleared up if it is doubtful, and if a calculus is felt it may be pressed on. If these measures fail, operation should be undertaken without further delay.

J. Hutchinson² advocated a policy of non-interference in gall-stone obstruction, and urged the use of anaesthetics, opium, and rectal injections with air or fluid to diminish spasm and assist in the passage of the calculus. Massage has been followed by cure.

In Martin and Brouardel's³ case massage was employed on the sixth day of obstruction and on the next day a large gall-stone and ten smaller stones were evacuated.

IV. THE INFLAMMATORY AND INFECTIVE CHANGES SET UP BY GALL-STONES include a large number of irregular manifestations and results, and will be conveniently described under the various headings of changes in connexion with—(A) The gall-bladder; (B) the cystic duct, (C) the common bile-duct; (D) the ampulla of Vater; and (E) the various fistulae.

SYNOPSIS

(A) Gall-bladder: cholecystitis; ulceration; haemorrhage; scars, hour-glass contraction; perforation; pericholecystitis adhesions.

(B) Cystic duct: swelling; obliteration; diverticulum.

(C) Common bile-duct: intermittent hepatic fever; extension to pancreatic duct—pancreatitis, cysts; extension to portal vein—pyelephlebitis.

(D) Ampulla of Vater.

(E) Fistulae.

(A) **Inflammatory and Infective Changes in the Gall-bladder.**—The presence of gall-stones, which are due to comparatively mild inflammation of the gall-bladder, disposes to fresh infection and thus to cholecystitis and to a vicious circle. No doubt gall-stones also favour persistence of the original infection, and thus are important in connexion with typhoid "carriers."

¹ Mayo Robson. *Diseases of the Gall-bladder and Bile-ducts*, p. 157, 1904.

² Hutchinson, J. *Arch. Surg.*, Lond., 1890-91, ii, 4.

³ Martin et Brouardel. *Bull. Soc. Anat. Paris*, 1875, i, 570.

Mieczkowski,¹ from examination of the bile of 15 patients whose gall-bladders were healthy and were aspirated during laparotomy for other conditions, concludes that human bile is sterile. In 23 cases of cholelithiasis investigated by him the bile was infected in 18. Gall-bladders containing gall-stones, therefore, are usually infected and are thus prone to fresh attacks of cholecystitis.

Cholecystitis.—Inflammation of various degrees of severity may supervene in a gall-bladder containing gall-stones. There may be acute infective cholecystitis, serous, sero-fibrinous, or purulent, which may go on to ulceration and perforation or gangrene; or there may be chronic serous or purulent cholecystitis, the latter condition being often spoken of as empyema of the gall-bladder. Descriptions of these various forms of cholecystitis are given elsewhere (*vide* p. 609). Acute cholecystitis may set up local peritonitis, and by paralysing the peristaltic movements of the intestines, may imitate acute intestinal obstruction.

Ulceration of the mucous membrane of the gall-bladder may give rise to: (1) Changes in the gall-bladder—(a) haemorrhage; (b) scars; (c) hour-glass contraction and diverticula. (2) Perforation of the gall-bladder—(a) into the general cavity of the peritoneum; (b) into part of the peritoneum shut off by adhesions; (c) into the liver; (d) into other adjacent structures, such as bile-ducts, portal vein, hepatic artery; (e) into the duodenum, colon, etc. (*vide* *Fistulae*, p. 766).

(1) *Changes in the Gall-bladder.*—(a) *Haemorrhage.*—An ulcer due to cholecystitis may cause haemorrhage into the gall-bladder. This may depend on erosion of a small vessel in the wall of the gall-bladder, but in rare instances ulceration of the gall-bladder may involve the hepatic artery and give rise to an aneurysm (*vide* p. 45) which may subsequently rupture.

(b) *Scars.*—As a result of the healing of an ulcer in the mucous membrane of the gall-bladder a scar results. In 343 cases of cholelithiasis tabulated by Schloth² there were 14 with cicatrices. These are usually in the fundus or close to the origin of the cystic duct. Their site depends to some extent on the mechanical irritation of the calculus. It may be pointed out, however, that what looks like a scar on the surface of the gall-bladder may in reality be a very early stage of primary carcinoma.

(c) *Hour-glass Contraction.*—Cicatrization following inflammation and ulceration may lead to hour-glass contraction. The gall-bladder may thus become divided into two compartments communicating by a narrow orifice, one or both of which may contain calculi. The orifice between the two may become closed, so that the fundus no longer communicates with the cystic duct.

Kehr³ records such a case in which one compartment contained pus, the

¹ Mieczkowski. *Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1900, vi, 307; Abstract in *Am. Journ. Med. Sc.*, 1902, cxxiii, 372.

² Schloth. *Diss.*, Würzburg, 1887. Quoted by Naunyn.

³ Kehr. *Diagnosis of Gall-stone Disease*. American transl., p. 48, 1901.

Among 530 cases of gallstones operated upon Rovsing found
that ⁱⁿ 314 the gall bladder bile was sterile and in 216 infected, and
argues that the infection is secondary.

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I have seen bilirubin-calcium calculi in
the proximal sacculus and cholesterol containing
calculi in the distal.

Rovsing, T. Acta chir. Scandinav., 1923, Lvi, 103.

other clear bile. In Donald's¹ case the peripheral part contained mucus only.

Courvoisier collected 15 examples of hour-glass gall-bladder, and others have been recorded since his monograph was published in 1890. Much the same appearance is seen in cases in which a number of septa from the walls of the gall-bladder form ridges between a succession of calculi. In this way the gall-bladder may become divided into several compartments communicating by narrow orifices. Barnard² described a gall-bladder containing four such compartments, one of which opened into the duodenum.

(2) *Perforation of the Gall-bladder.*—(a) *Into the General Cavity of the Peritoneum.*—Perforation or rupture of an inflamed gall-bladder allows bile and even gall-stones to escape into the general cavity of the peritoneum and sets up severe and usually fatal peritonitis. This is especially seen in phlegmonous and gangrenous cholecystitis (*vide* pp. 621 and 623).

(b) *Into a Localised Part of the Peritoneum cut off by Adhesions.*—A local abscess formed in connexion with perforation of a calculous gall-bladder into part of the peritoneum previously cut off by adhesions may contain gall-stones, and may open in one or more of a number of different situations, such as the duodenum, stomach, on the surface of the abdomen, etc. (*vide* Biliary Fistulae), or present as a subphrenic abscess, or give rise to an empyema on the right side.

(c) *Ulceration of the Gall-bladder into the Substance of the Liver.*—Ulceration of the gall-bladder may extend directly into the liver; it may then give rise to an abscess cavity in the liver communicating with the gall-bladder, or to haemorrhage into the gall-bladder. This, however, is very rare.

Arbuthnot Lane³ described a case in which the liver shewed an encysted cavity, containing calculi and opening into the gall-bladder; and a second case⁴ in which the gall-bladder, probably containing a calculus, exhibiting on its anterior surface a rupture extending into the liver and giving rise to profuse haemorrhage into the gall-bladder.

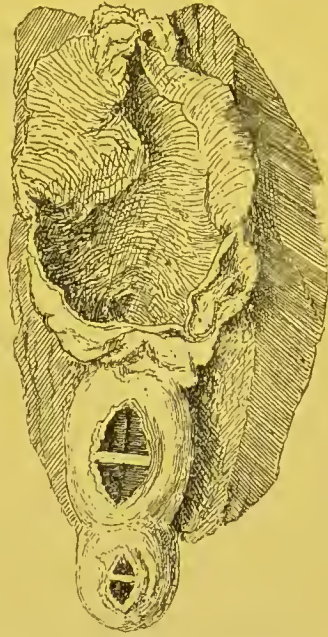


FIG. 107.—Hour-glass contraction of gall-bladder. The fundus, which communicates with the remainder of the gall-bladder through a minute orifice admitting a bristle, contains two calculi, one above the other, partially separated from each other by a septum from the wall of the gall-bladder. (Drawn by Dr. G. H. Goldsmith.)

¹ Donald. *Glasgow Med. Journ.*, 1898, N.S., xlix, 348.

² Barnard, H. L. *Ann. Surg.*, 1902, xxxvi, 161.

³ Lane. *Lancet*, Lond., 1893, ii, 874.

⁴ Idem. *Trans. Clin. Soc.*, Lond., 1895, xxviii, 160.

(d) Ulceration of the gall-bladder may extend into the common bile-ducts, portal vein, and hepatic artery in the lesser omentum. These extremely rare events are also referred to under the head of biliary fistulae (*vide* p. 772). Ulceration of the hepatic artery may give rise to an aneurysm (*vide* p. 45).

Pericholecystitic Adhesions.—Inflammation of a calculous gall-bladder readily gives rise to adhesions which unite it to adjacent organs, especially the pyloric end of the stomach and the duodenum. According to the thickness and density of the adhesions symptoms of a varying degree of intensity are induced. In the slighter cases there is pain after food, or “adhesion dyspepsia,” due to interference with the gastric movements and to dragging on adhesions. Dense adhesions may so constrict or kink the pylorus or duodenum that pyloric obstruction is induced, and the case may closely resemble carcinoma of the pylorus with dilatation of the stomach (Mayo Robson,¹ Tuffier and Marchais,² Thomas,³ Page,⁴ Villard⁵). In many cases the symptoms come on very gradually, and a considerable time after definite symptoms of gall-stones, so that their causation is obscure. In a few cases haematemesis has been recorded, thus making the resemblance to primary gastric disorder even more definite. When dieting and thorough medical treatment fail to relieve these cases of pyloric stenosis due to adhesions set up by calculous cholecystitis, exploratory laparotomy is justified.

Dr. Fütterer, of Chicago, kindly sent me photographs of the gall-bladder in a case in which old adhesions between a calculous gall-bladder and the pylorus conveyed carcinoma from the pylorus to the gall-bladder.

When a gall-stone has ulcerated into the duodenum the cicatricial contraction which follows may give rise to stricture of the duodenum and so to obstruction.⁶ Bland-Sutton⁷ mentions a case of hour-glass stomach which may have been produced in this manner. In some instances adhesions due to past cholecystitis may form bands which constrict the colon or the small intestine and so produce acute intestinal obstruction.

Niles⁸ reported a case of stenosis of the hepatic flexure by pericholecystitic adhesions which was cured by dividing the adhesions and removing 60 small calculi from the gall-bladder.

Adhesions may be formed between the gall-bladder and the vermiform appendix as the result of inflammation of the gall-bladder. This may explain why cholelithiasis often gives rise to pain suggesting appendicitis.

¹ Mayo Robson. *Trans. Clin. Soc.*, Lond., 1894, xxvii, 1.

² Tuffier et Marchais. *Rev. de chir.*, Paris, 1897, xvii, 100.

³ Thomas. *Rev. méd. de la Suisse Rom.*, Genève, 1897, xvii, 5.

⁴ Page, F. *Brit. Med. Journ.*, 1897, i, 205.

⁵ Villard. *Lyon méd.*, 1902, xcix, 737.

⁶ Labadie-Lagrave et Magdelaine. *Rev. gén. de clin. et de thérap.*, Par., 1898, xii, 401.

⁷ Bland-Sutton. *Clin. Journ.*, Lond., 1906-7, xxix, 18.

⁸ Niles, H. D. *Ann. Surg.*, 1902, xxxv, 344.

(B) **Results of Inflammation in the Cystic Duct.**—The impaction or passage of a calculus, especially an angular one, along the cystic duct may set up severe inflammatory changes, ulceration, and subsequently cicatricial contraction of the duct. In some cases inflammatory adhesions around the cystic duct may constrict the neighbouring common hepatic and common bile-duets. A calculus when impacted may lead to ulceration and bulging of the walls of the duct, so that it becomes eneysted in a diverticulum.

In a woman who died of bronchitis in St George's Hospital the liver was very freely movable and shewed evidence of tight lacing. The neck of the gall-bladder was long, and just at the commencement of the cystic duct there was a recess containing a gall-stone (*vide* Fig. 108). The gall-bladder was not dilated, and bile could easily be driven from the gall-bladder into the duodenum.

A calculus in such a diverticulum may press on the cystic duct (W. W. Cheyne¹), or possibly on the common hepatic duct.

A calculus may ulcerate out of the duct and give rise to a localised abscess in the immediate neighbourhood. A calculus in the cystic duct may set up inflammation which spreads into the common duct and so causes jaundice.

(C) **Inflammation and Infective Changes in the Common Bile-duct.**—The inflammation of the common bile-duct associated with the presence of a gall-stone may possibly be an extension of the cholecystitis which originally drove the calculus out of the gall-bladder, but probably in most cases the presence of the calculus favours an ascending infection of the common bile-duct from the duodenum. Calculi in the common duct frequently set up the infective condition described below as intermittent hepatic fever. It may also give rise to ulceration of the duct and to perforation and the formation of a local abscess, or to suppurative cholangitis (*vide* p. 671) and multiple abscesses in the liver.

Intermittent Hepatic Fever.—A characteristic result of calculi in the common bile-duct is a group of symptoms collectively described as intermittent hepatic fever. Its clinical features, first noted by Charcot,² and especially insisted upon by Osler,³ are now well recognised.

Anatomically the calculus "floats" near the lower end of the common bile-duct, which is often greatly dilated. The calculus is movable, and is said to exert a ball-valve action (Osler,⁴ C. Fenger⁵). In many cases the



FIG. 108—Gall-bladder with elongated neck and diverticulum at the commencement of cystic duct containing a calculus.

¹ Cheyne, W. W. *King's Coll. Hosp. Rep.*, 1897, iii, 94.

² Charcot. *Leçons sur les maladies du foie et des voies biliaires*, p. 178, 1877.

³ Osler. *Johns Hopkins Hosp. Rep.*, Balt., 1891, ii, 3. *Lancet*, Lond., 1897, i, 1319.

⁴ Idem. *Med. Times and Gaz.*, 1881, ii, 111.

⁵ Fenger, C. *Am. Journ. Med. Sc.*, 1896, cxi, 125.

dilatation of the duct around and above the gall-stone, which often lies in a pathologically dilated ampulla of Vater, allows bile to trickle past into the duodenum. The gall-stone may make the biliary papilla project into the duodenum. The common and other bile-ducts are dilated, often greatly, and their walls are thickened, but the mucous membrane, though inflamed, is usually free from ulceration. Adhesions over the convexity of the liver, due to past attacks of perihepatitis, are common. The intra-hepatic bile-ducts may be dilated, and from pericholangitis there is increased fibrosis around them with some atrophy of the liver substance; this constitutes the condition often described as obstructive biliary cirrhosis (*vide* p. 331).

The gall-bladder is usually small, thickened, and contracted from past cholecystitis in accordance with Courvoisier's¹ well-known law that in jaundice due to gall-stones the gall-bladder is small, whereas in icterus due to the pressure of a tumour on the ducts the gall-bladder is distended. There are frequently adhesions between the gall-bladder and the adjacent viscera, especially the omentum, stomach, and the transverse colon. There may, or may not, be gall-stones in the gall-bladder. The head of the pancreas is commonly enlarged from chronic interstitial pancreatitis.

Charcot regarded the fever as due to absorption of poisons from the bile-ducts. Netter and Martha,² Abbott, and Pick³ found micro-organisms, especially the colon bacillus, in the ducts. Budd⁴ drew an analogy between urethral fever following catheterisation and intermittent hepatic fever. Murchison and Ord⁵ regarded the fever as the reflex result of irritation exerted by the calculus.

The striking intermissions in the symptoms may possibly depend on the micro-organisms which have set up acute swelling of the mucous membrane of the duct and biliary obstruction, passing away into the duodenum. Or, on the other hand, periodic intervals of immunity may be developed with the result that the symptoms disappear, only to reappear when, immunity being exhausted, the micro-organisms, which in the interval, though present, have remained latent, set up a fresh and acute cholangitis.

Clinical Picture.—The symptoms may come on many years after the original attack of cholecystitis which gave rise to the gall-stone, or there may be recurrent attacks of biliary colic eventually terminating in intermittent hepatic fever.

W. Moore⁶ reported a case in a woman aged fifty-four who first had jaundice when nineteen years old. For twenty-five years she had had yearly attacks of biliary colic, which recently had been accompanied by jaundice and shivering. Recovery followed removal of a calculus from the common bile-duct and 21 calculi from the gall-bladder.

¹ Courvoisier. *Pathologie u. Chir. d. Gallenwege*, 1890.

² Netter et Martha. *Arch. de physiol. norm. et path.*, Paris, 1886, 3. s., viii, 7.

³ Pick, F. *Verhandl. d. XV. Congr. f. inn. Med.*, Berl., 1897, xv, 468.

⁴ Budd. *Diseases of the Liver*, p. 376, 3rd ed., 1857.

⁵ Ord, W. M. *Brit. Med. Journ.*, 1887, i, 496.

⁶ Moore, W. *Intercolon. Med. Journ. Australas.*, 1899, iv, 407.

Bile-pigment and bile salts
may be absent from the urine
between the attacks, or bile
salts only be present. There
is excess of urobilin when
the liver cells are infected.

There may not be any history of colic from which to date the passage of the calculus into the common duct, so that, especially in old people, the onset of jaundice may be gradual and painless, as in malignant disease. The clinical aspect of these cases may be summed up in the occurrence of ague-like attacks of fever, pain, rigors, and increase in the jaundice, while in the intervals the patients are fairly well and even able to live their ordinary lives. The disease may continue for years, but eventually may terminate in suppurative inflammation of the ducts, the liver, or in the neighbourhood of the calculus.

The attacks, which sometimes closely resemble ague in their periodicity, are accompanied by fever, the temperature going up as high as 103° , rigors, and sweating. The pain is felt in the region of the liver and epigastrium, and may be as severe as that of ordinary biliary colic and necessitate relief by hypodermic injection of morphine. There may be tenderness in the back, close to the tenth dorsal spine on the right side. Jaundice may be transient, intermittent, or disappear after being distinct, or be entirely absent; it was absent in 25 per cent of Moynihan's¹ cases. It is commonly slight during the intervals, but during the attacks it becomes more intense and may be accompanied by itching of the skin; but I have seen most intense pruritus in the absence of jaundice. Vomiting is often present during the attack, and dyspepsia and gastric pain are frequently troublesome. These symptoms are often the most prominent and sometimes the only ones; many cases indeed are regarded as purely gastric. There may be so much pyloric obstruction as to suggest organic stricture due to pericholecystic adhesions; in some instances no adhesions are found on exploration and the pyloric obstruction may be assumed to be due to spasm. I have seen sprue-like diarrhoea associated with attacks of colic and cured by removal of a calculus from the common bile-duct. The liver may be somewhat enlarged and tender during an attack, but the gall-bladder cannot be felt. The spleen is usually palpable during the attacks. There is a leucocytosis during the attack, but not in the intervals (Pick). A Temporary glycosuria has been thought to be due to the action of poisons, absorbed from the duct, on the islands of Langerhans, and has been known to disappear when thorough drainage was established (Mansell Moullin²). ~~There is excess of urobilin in the urine.~~

Complications.—Inflammation and ulceration of the common bile-duct in rare instances lead to cicatricial contraction of the duct. Examples of this curiously infrequent sequel are given on p. 661.

~~Kehr³ records complete obliteration of the common bile-duct at its junction with the cystic duct due to this cause.~~ dy

Suppurative cholangitis may supervene, and spread widely into the liver, and into the pancreas (*vide* p. 675).

Diagnosis.—The periodicity of the febrile attacks may closely imitate

¹ Moynihan. *Brit. Med. Journ.*, 1912, i, 347.

² Mansell Moullin. *Lancet*, Lond., 1907, i, 1645.

³ Kehr. *Diagnosis of Gall-stone Disease*, American transl., p. 48, 1901.

malaria, but there is no reaction to quinine and the malarial parasite is not found in the blood. The presence of jaundice in the intervals and its intensification during the attacks should always suggest cholelithiasis. ~~The diagnosis of gall-stones by x-rays cannot be relied upon, as no shadow is given unless the calculi contain lime salts. A negative result is therefore of no value.~~

It is important to distinguish the condition from suppuration of the bile-ducts, which, as has been pointed out, may supervene on intermittent hepatic fever. In suppurative cholangitis the fever is continuous, the paroxysms are more frequent, and there are no intervals of comparatively good health; the patient is much worse, the liver is more enlarged, the gall-bladder may be palpable, and the jaundice is not so marked.

In hepatic abscess the fever is continuous, the liver is more enlarged, and leucocytosis, if present, is constant and does not pass away as it does in intermittent hepatic fever.

In malignant disease the liver is more enlarged and often irregular; the course of the disease is more rapid, and, though there may be fever, it is not periodic. In malignant disease pressing on the ducts, as in carcinoma of the head of the pancreas, the jaundice is deep and the motions are devoid of stercobilin. The gall-bladder is generally distended and the temperature is not raised. Cammidge's¹ tests are of value in the differential diagnosis between stone in the common duct and malignant disease of the head of the pancreas:—

	Stone in Common Duct.	Carcinoma of Pancreas.
Pancreatic reaction.	Positive in 66 per cent.	Negative in 66 per cent.
Urobilinuria.	Present.	Rare.
Crystals of calcium oxalate.	Present.	Rare.
Fat in the faeces.	Proportion of "saponified" exceeds that of "unsaponified fat."	Proportion of "saponified" less than, or equal to, that of "unsaponified fat."
Occult blood in Faeces	Absent	Present

From chronic cholangitis due to infection of the ducts with micro-organisms of no great virulence the diagnosis is difficult; but the pain and intermittent fever are more severe and prominent in the cases complicated by cholelithiasis; and the non-calculous cases react better to urotropin.

Hypertrophic biliary cirrhosis in rare instances comes on acutely and might imitate a calculus passing into the duct; the periodic attacks of

¹ Cammidge. *Proc. Roy. Soc. Med.*, Lond., 1910, iii (Med. Sect.), 163.

19 The diagnosis of gallstones by x-rays is becoming increasingly important; positive or direct evidence of gallstones fails when there is a pure cholesterol stone, so that,

and PFAHLER

Pancoast, considered that a conservative estimate

that ^{about} 50 per cent. of gallstones can be detected by x-rays, but ~~some x-ray proof that the percentage~~ is high as 75 per cent. By inflating the positional cavity with oxygen, opaque gallstones are readily seen, and translucent ones appear as translucent within the gallbladder shadow as they are more translucent than bile or mucus (Roberts).

The main radiological difficulty is to distinguish between renal calculi and gallstones, and in cases of such a nature the examination is not complete without lateral radiography and pyelography (Knox).

indirect evidence, namely deformity of the duodenal cap or hepatic flexure of the colon enables a diagnosis to be made in 85 to 95 per cent. (Leonard and George).

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Cholecystography by making the gall bladder visible under x-ray by means of tetra-iodophenolphthalein, in bromine-ly or, better, as constitutional reactions are thus avoided, by or tetrabromophenolphthalein

the mouth in pills coated with salol (Graham and Cole; Carman; Whitaker, Millikin and Vogt). Failure of the gall bladder to fill is a sign of a pathological state and gall stones are shown by a mottled appearance.

PANCOAST. Trans. Col. Phys., Phila., 1917, XXXIX, 257.

PFAHLER Journ. Am. Med. Assoc., Chicago, 1918, LXXI, 1951

ROBERTS, J. Brit. med. Journ., 1929, II, 742.

KNOX, R. Acta Radiologica, Stockholm, 1924, III, 267.
(Scandinavian)

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Graham and Cole. Journ. Amer. Med. Assoc., Chicago 1924, LXXXII, 613, 1777.
CARMAN, R. D. Lancet, Lond., 1925, II, 67.
Whitaker, Millikin, and Vogt. Surg. Gyn. and Obstet., Chicago 1925, XL, 847.

fever, pain, and increased jaundice are much less severe in biliary cirrhosis; further, splenic enlargement is prominent in biliary cirrhosis, and is absent in the intervals between the attacks in intermittent hepatic fever.

The prognosis is rather bad on medical or expectant treatment, as suppuration may supervene in the bile-ducts, the liver itself, or in the neighbourhood. In 10 cases tabulated by Osler,¹ spontaneous recovery occurred in 5. The outlook is much better if the cases are submitted to operation and the stone or stones removed from the common bile-duct. I have, however, seen persistent diarrhoea like sprue prove fatal a considerable time after successful operation. This case shewed chronic pancreatitis and two ulcers in the duodenum.

Treatment.—In cases in which the attacks occur at considerable intervals medical treatment should be tried. The patient should take a light, digestible diet, avoid stimulants, and keep the bowels open. The dieting of cases with gastric pain is often very disappointing, a result which can hardly be wondered at since the pain and dyspepsia are largely reflex and depend on the presence of the calculus in the duct, or possibly on adhesions around the pylorus. Carlsbad water at home, or better a cure there or at one of the spas mentioned on p. 779 is advisable, and it is well to increase the flow of bile over the calculus in the hope of dissolving its surface sufficiently to allow it to slip into the duodenum. Urotropin combined with salicylate and bicarbonate of sodium should be given to increase the flow of bile and to inhibit bacterial activity; if there is itching, much jaundice, or haemorrhages calcium salts should be given. For the treatment of pruritus see p. 567. hvs

For the pain hot applications, fomentations, or poultices may be tried, but in many cases morphine is required and there is the danger that the habit may be acquired. Antipyrin and phenacetin may be tried, or a mixture containing belladonna and spiritus chloroformi to allay spasm. Turpentine and ether have been given with the same object. With the exception of morphine, these measures often fail. Massage is unsafe, and olive oil by the mouth of no real use so far as removal or solution of the calculus is concerned. In cases in which the patient cannot be operated upon, some prolongation of the intervals between the attacks may follow injection of autogenous vaccines of *B. coli*, isolated from the faeces and proved by the agglutination reaction or the opsonic index to be the infecting agent. I have seen a good effect in one case.

If no improvement follows medical treatment, *operative measures* should be advised before the patient loses too much flesh or gets deeply jaundiced, as these conditions render operation dangerous. Further, from continued infection of the ducts the liver becomes damaged (pericholangitic fibrosis and atrophy); the irritation of other calculi in the gall-bladder favours primary carcinoma; suppurative cholangitis may supervene; and in long-standing cases dense adhesions may form around the gall-bladder and ducts and make operation both more difficult and dangerous. Generally

¹ Osler. *Lancet*, Lond., 1897, i, 1319.

speaking, the time devoted to unsuccessful medical treatment should not exceed two months, but each case must be considered on its merits. The most radical and effective treatment is laparotomy and removal of the stone from the common duct. Probably in some cases operation short of this has done good; mere manipulation of the ducts may drive a softened stone into the duodenum and effectually remove it.

A woman aged fifty-four who had had about 20 attacks within the year came under my care in 1896 in St. George's Hospital. During an attack the temperature went up to 104° , jaundice became more marked, bile appeared in the urine, and there was marked tenderness over the common bile-duct. Mr. Sheild explored the abdomen, broke down adhesions around the common bile-duct, which felt thickened, but did not open the duct, as no calculi were palpable. After this the patient remained free from any further attacks.

Extension of Inflammation and Infection to the Pancreas.—Gall-stones in the common duct, especially when in their usual situation, viz. the lower end, readily give rise to inflammation of Wirsung's duct of the pancreas and pancreatitis. The inflammation may spread (1) from the bile-duct into Wirsung's duct, (2) from the duct by continuity into the pancreas, (3) by the lymphatics (Maugeret¹).

Thirty-two cases of acute pancreatic lesions, such as haemorrhage, suppuration, acute pancreatitis, have been collected by Opie² in which gall-stones were present. Of 105 cases of acute pancreatitis collected by Egdahl³ 44 were associated with gall-stones. I had previously called attention, though on a much smaller number of cases, to the production of pancreatitis by cholelithiasis.⁴

The following list of changes in the pancreas, due to cholelithiasis, is based on Mayo Robson's⁵ classification: (a) Changes in the ducts: catarrh, suppuration, lithogenic inflammation. (b) Changes in the pancreas: (i) acute; catarrhal, haemorrhagic, gangrenous, suppurative inflammation; (ii) subacute; localised abscess; (iii) chronic, interstitial pancreatitis.

The production of suppuration in the pancreas by calculi in the common bile-duct was described in 1882 by Norman Moore.⁶ The following case illustrates this point:—

A man, aged sixty-three, who had had an attack of jaundice and abdominal pain five years before, was seized with abdominal pain a week before his death. He was admitted to St. George's Hospital in a jaundiced, drowsy, and exhausted condition. His temperature was 101° , there was tenderness in the upper part of the abdomen, and he sweated profusely, without any shivering. He died from exhaustion within twenty-four hours of admission. At the necropsy there were three large crumbling calculi in the common bile-duct, which was dilated to the size of one's thumb and had a granular, thickened condition of its mucous

¹ Maugeret. *Thèse de Paris*, 1908.

² Opie. *Am. Journ. Med. Sc.*, Phila., 1901, cxxi, 27.

³ Egdahl. *Johns Hopkins Hosp. Bull.*, Balt., 1907, xviii, 130.

⁴ Rolleston. *Trans. Path. Soc.*, Lond., 1898, xlix, 149.

⁵ Mayo Robson. *Lancet*, Lond., 1904, i, 770.

⁶ Moore, N. *Trans. Path. Soc.*, Lond., 1882, xxxiii, 186.



membrane. The cystic duct was dilated, there was an ulcer in the fundus of the gall-bladder, which contained bile-stained mucopus but no calculi. The intrahepatic ducts were slightly dilated and shewed pericholangitic fibrosis, but there was no suppuration. The pancreatic duct contained discoloured pus, and there were spots of suppuration in the pancreas.

Pancreatitis may cause inflammation of the peritoncum of the lesser sac and so lead to closure of the foramen of Winslow and to an inflammatory exudate. Cholelithiasis may thus set up a peripancreatic effusion in the lesser sac, the contents being either serous or purulent. Many so-called pancreatic cysts are of this nature. The following case is of interest in this connexion :—

A man, aged twenty-five, was seized two weeks before his death with pain, never very acute, in the lower abdomen, and vomiting, which persisted until his death. He had never had jaundice, a blow on the abdomen, or any serious illness. An indistinct tumour was felt in the left hypochondrium, with the stomach resonance above it. At the necropsy there were 59 small calculi in the gall-bladder and one in the cystic duct, which was very long and joined the common hepatic duct $\frac{3}{4}$ inch above the biliary papilla. The cystic duct was inflamed, and it seemed possible that inflammation had spread from it to the pancreas. There was a localised effusion distending the lesser sac of the peritoneum into a cyst as large as one's head, the foramen of Winslow being closed. The pancreas shewed acute pancreatitis under the microscope. This peripancreatic cyst was evidently secondary, just as pleurisy is to pneumonia, to acute inflammation of the pancreas, which in its turn was associated with cholelithiasis.¹

Chronic pancreatitis from extension of inflammation from the common bile-duct *via* Wirsung's duct is a frequent accompaniment of calculi in the lower part of the common bile-duct. Chronic pancreatitis does not occur in every case in which a calculus occupies the lower end of the common bile-duct; the determining factors are the anatomical relations (*a*) of the common bile-duct and Wirsung's duct, and (*b*) of the common bile-duct to the head of the pancreas (*vide* also p. 559). In some cases the common bile-duct and Wirsung's duct open separately into the duodenum, and in these circumstances inflammation is not likely to spread from the bile-duct to the pancreas. In 62 per cent of bodies the common bile-duct is embedded in the head of the pancreas, and in these cases inflammation readily extends from the duct into the head of the pancreas; in the cases in which the anatomical relation of the two is not so intimate, the duct running behind the head of the pancreas in 38 per cent of bodies (Helley²), chronic pancreatitis is not so likely to supervene (*vide* Robson and Cammidge³). The head of the pancreas may become so hard that when felt during the course of an operation for gall-stones the surgeon may assume that there is malignant disease of the head of the pancreas and abandon the operation.

¹ Rolleston. *Trans. Path. Soc.*, Lond., 1898, xlix, 145.

² Helley. *Arch. f. mikr. Anat.*, Bonn, 1898, lii, 773.

³ Robson and Cammidge. *The Pancreas, its Surgery and Pathology*, p. 365, 1907.

The inflammatory changes thus started may progress, even though the calculi which caused it have passed into the duodenum (Mayo Robson,¹ Barling²). Subsequently the enlarged head of the gland undergoes atrophy from cicatricial contraction of the newly formed fibrous tissue, and imitates a hard, slowly growing carcinoma of the head of the pancreas by compressing the common bile-duct and producing chronic jaundice.

The treatment of such cases is to establish free drainage for the gall-bladder; if this is kept up for some time, the condition of the pancreas will improve. It seems safer to drain the gall-bladder externally and not to do cholecystenterostomy.

Pylephlebitis.—Inflammation of the bile-ducts may give rise to suppurative pylephlebitis. The inflammation may spread to the main trunk of the portal vein or to its intrahepatic branches. In some instances the infection may spread to the portal vein by the lymphatics or by the small veins of the bile-ducts which open into the branches of the portal vein. This subject is fully discussed elsewhere (*vide* p. 72).

(D) **Inflammatory Effects of a Calculus in the Ampulla of Vater.**—A calculus in the ampulla Vateri often obstructs the main pancreatic duct, but as the latter usually communicates in the pancreas with the accessory or Santorini's duct, the pancreatic secretion is not prevented from entering the duodenum. But the presence of a calculus in the ampulla of Vater favours the spread of infection into the pancreas and very commonly causes chronic pancreatitis. As the result of continued chronic pancreatitis, cicatricial contraction may result and compress both the ducts, giving rise to retention of the secretion, dilatation of the ducts, and sometimes to the formation of cysts in the gland. The chronic interstitial pancreatitis very seldom causes glycosuria or diabetes.

(E) **Biliary Fistulae.**—Abnormal passages between the gall-bladder and bile-ducts and other viscera or the outside of the body are in the great majority of instances due to gall-stones and inflammatory processes accompanying them. External fistulae may result from other causes, such as operations on the gall-bladder and ducts, or on hepatic abscesses and hydatid cysts. The following remarks on biliary fistulae refer to those associated with calculi.

External or Cutaneous Biliary Fistulae.—Suppuration in the gall-bladder may eventually discharge through the abdominal walls. This form of biliary fistula has been most frequently reported.

Naunyn³ collected 184 examples out of a total of 384 biliary fistulae due to cholelithiasis, the next most frequent form of fistula being that between the gall-bladder and duodenum (108).

The communication between the gall-bladder and the opening in the abdominal wall is often by a long fistulous tract which may be tortuous and difficult to follow. The fistula may be the opening of an abscess in

¹ Mayo Robson. *Lancet*, Lond., 1900, ii, 236.

² Barling, G. *Brit. Med. Journ.*, 1900, ii, 1766.

³ Naunyn. *On Cholelithiasis*, p. 143. Transl. New Sydenham Soc., 1896.

the neighbourhood of the gall-bladder or may lead directly into the suppurating gall-bladder.

External biliary fistulae usually open near the umbilicus; this depends partly on the vicinity of the gall-bladder and partly on the fact that the falciform ligament ~~seems to guide~~ the pus in this direction. Not uncommonly the opening is in the right hypochondrium. In rare instances the ~~pus may be discharged~~ abscess ^{1 point} in the right iliac fossa ^{and 1/2} which imitates an appendicular abscess.

Gibbon¹ explored a spontaneous sinus in the right iliac fossa, $\frac{3}{4}$ inch below and $2\frac{1}{2}$ inches internal to the anterior-superior spine of the ilium, and removed 52 calculi, after which the fistula healed.

In very rare instances a biliary fistula may be established in the thigh. Porges² ~~has~~ recorded the discharge of gall-stones from such a fistula.

Fistulae between the Biliary and Gastro-intestinal Tracts.—Often, when this condition is found after death, there have been no clinical manifestations of the process, such as intestinal obstruction from a large gall-stone, or the passage of a calculus in the faeces, and its existence has not been suspected during life. A fistula may be suspected when a large calculus is passed by the bowel, but this often occurs when no absolute proof of a fistula is forthcoming.

In 111 cases in which a large calculus, viz. one the size of a nut, was passed by the bowel, the method by which it gained entrance into the bowels was quite unknown in 69 (Le Roy³).

Duodenal fistulae are the most frequent. In Naunyn's list of 384 biliary fistulae due to cholelithiasis the duodenum was involved in 108. As a rule the communication is between the fundus of the gall-bladder and the duodenum, but in a certain number of cases a calculus ulcerates through the walls of the common bile-duct into the first part of the duodenum, above the biliary papilla.

Cholecysto-duodenal Fistulae.—This form was present in 93 out of the 108 cases mentioned above. The fundus of the gall-bladder communicates with the first part of the duodenum. The process of ulceration may cause severe gastro-intestinal haemorrhage. Such cases may easily be misinterpreted and regarded as simple gastric or duodenal ulcer. Jaundice is absent as a rule, and if present is due to some complication.

A patient with impaction of a gall-stone in the common duct and a cholecysto-duodenal fistula had transient jaundice two months before death. The passage of a gall-stone into the common duct was thought to have both caused the jaundice and, by raising the pressure of bile in the gall-bladder, to have driven another calculus in the gall-bladder through a commencing cholecysto-duodenal

¹ Gibbon, J. H. *Phila. Med. Journ.*, 1901, vii, 128.

² Porges. *Wien. klin. Wchnschr.*, 1900, xiii, 597.

³ Le Roy, C. *Thèse de Paris*, 1902, No. 474.

fistula, and by thus providing an outlet for the bile to have removed the jaundice (Barnard¹).

In some instances cicatrization of the fistulous communication may lead to stricture of the duodenum and to symptoms of pyloric obstruction. Dense adhesions between the gall-bladder and the duodenum may imitate malignant disease even when the parts are exposed during an exploratory laparotomy. Primary carcinoma may occur in the gall-bladder after the formation of the fistula (*vide* case on p. 638). The mucous membrane around the fistulous opening in the duodenum may become extensively ulcerated and set up persistent vomiting; this may occur without any cicatricial stenosis of the duodenum or pylorus.

A calculus may ulcerate out of the gall-bladder, but fail to pass into the duodenum; the end of the calculus which projects into the intestine may be white, the pigment having been removed by the action of the acid contents of the duodenum (Barnard). So much cicatricial contraction may be set up around the duodenum that obstruction results. A case of this kind is reported by Labadie-Lagrave and Magdelaine.² Occasionally an abscess, formed around a gall-stone which is ulcerating out of the gall-bladder or common bile-duct, discharges in several directions and a complicated fistula results, with openings into the duodenum, stomach, and gall-bladder.

A woman aged fifty-four years died in St. George's Hospital after removal of the right big toe. She had diabetes of pancreatic origin and was jaundiced. The gall-bladder was shrivelled up on a gall-stone, and communicated by a fistula with the first part of the duodenum. There was a soft, crumbling calculus the size of a pigeon's egg in the lower part of the common bile-duct. Near this calculus, but not in actual continuity, there was an abscess, partly in the head of the pancreas and partly in the lesser omentum and left lobe of the liver. This abscess communicated by two small openings with the duodenum, and by two more fistulae with the stomach on its posterior wall. The pancreas was markedly fibrotic.

Choledocho-duodenal Fistula.—A communication between the common bile-duct and the first part of the duodenum is probably commoner than is believed. Naunyn points out that in some cases in which the calculus is seen projecting into the duodenum the orifice is not the biliary papilla, as is often assumed merely because there is an opening there, but a fistulous passage. Naunyn thinks it not improbable that fistulae between the duodenum and the common bile-duct are as common as those between the duodenum and gall-bladder. But of his 108 collected cases of duodenal fistulae 15 only were between the common duct and the duodenum, and the remaining 93 between the gall-bladder and the duodenum.

Biliary Gastric Fistulae.—Communications between the stomach and biliary tract are very rare, and when they do occur, are in some instances

¹ Barnard. *Ann. Surg.*, 1902, xxxvi, 161.

² Labadie-Lagrave et Magdelaine. *Journ. des praticiens*, June 25, 1890.

^ and muscular hypertrophy of
the pylorus (Hale White; Mader);

Hale White. Trans. Path. Soc., Lond., 1886, xxxvii, 280

Mader. Quoted by Thompson. Trans. Amer. Surg. Assoc., 1912, xxx, 514.



due to an abscess, arising in connexion with the gall-bladder or ducts, opening into the stomach and also into the duodenum or colon, or both, as in a case reported by Voelcker.¹

Naunyn² quotes 12 gastrobiliary fistulae, 8 of which were between the gall-bladder and 4 between the ducts and the stomach. In Nicholls' case³ the patient was a woman aged eighty-five. In a complicated case reported by Lejonne and Milanoff⁴ there was a communication between the stomach and the gall-bladder, and a second fistula between the common bile-duct, which contained a calculus, and the first part of the duodenum. The gall-bladder shewed primary carcinoma, but the fistulae probably depended on cholelithiasis. The patient was a woman aged eighty-seven years. Cholecystogastric fistulae due to gall-stones have also been recorded by Ochsner⁵ and Snively.⁶ In a case recorded by Carter⁷ a calculus was wedged in the pylorus like a cork.

A cholecystogastric fistula may be brought to light in separating dense adhesions during operations on cases without any symptoms of such a fistula.

In a woman aged sixty who had had attacks of gall-stone pain for fifteen months, lately very frequently, followed by slight jaundice and constant dyspepsia with frequent vomiting and loss of flesh, Mayo Robson⁸ found the stomach and gall-bladder firmly adherent. On separating the adhesions a fistula between the gall-bladder and stomach was found. The gall-bladder contained calculi.

Vomiting of gall-stones has been thought to be good evidence of a gastrobiliary fistula; but this is not convincing, for since bile is commonly regurgitated into the stomach in vomiting, small calculi should be too. When, as rarely happens, a large calculus is vomited, a gastrobiliary fistula probably exists.

Thompson⁹ recorded the case of a woman aged ninety-four who vomited a calculus the size of a nutmeg. Jeaffreson¹⁰ quoted a case in which a large calculus was vomited, and after death the stomach was found adherent to the gall-bladder. In 12 cases in which gall-stones were vomited there was only 1 in which a gastrocholecystic fistula was proved to exist (Murchison¹¹). Mayo Robson,¹² Nicholls, Kellett Smith and Bailey,¹³ Crooke,¹⁴ Johnson,¹⁵ Pfeifferberger,¹⁶ and others have reported more recent cases in which gall-stones were vomited.

¹ Voelcker. *Trans. Path. Soc.*, Lond., 1895, xlv, 78.

² Naunyn. *On Cholelithiasis*, p. 143. Transl. New Sydenham Soc., 1896.

³ Nicholls, A. G. *Montreal Med. Journ.*, 1898, xxvii, 829.

⁴ Lejonne et Milanoff. *Bull. Soc. Anat. Paris*, 1900, lxxv, 33.

⁵ Ochsner. *Ann. Surg.*, 1902, xxxv, 712.

⁶ Snively. *Journ. Am. Med. Assoc.*, Chicago, 1903, xl, 963.

⁷ Carter. *Brit. Med. Journ.*, 1911, i, 307.

⁸ Mayo Robson. *Ibid.*, 1903, i, 185.

⁹ Thompson. *Trans. Path. Soc.*, Lond., 1861, xii, 129.

¹⁰ Jeaffreson. *Brit. Med. Journ.*, 1868, i, 531.

¹¹ Murchison. *Diseases of the Liver*, p. 548, 1885.

¹² Mayo Robson. *Lancet*, Lond., 1897, i, 1526.

¹³ Kellett Smith and Bailey. *Liverpool Med.-Chir. Journ.*, 1902, xxii, 74.

¹⁴ Crooke. *Ibid.*, p. 76.

¹⁵ Johnson. *Montreal Med. Journ.*, 1909, xxxviii, 315.

¹⁶ Pfeifferberger. *Journ. Am. Med. Assoc.*, 1910, lv, 1024.

Cholecystocolic Fistulae.—A fistulous communication between the biliary tract and the colon is less frequent than one involving the duodenum as the result of cholelithiasis.

Naunyn gives 49 examples of fistulae between the gall-bladder and the colon and one between the common bile-duct and the colon.

An indirect result of gall-stones, namely, carcinoma of the gall-bladder, may cause a fistulous opening into the colon. Out of 9 cases of cholecystocolic fistulae mentioned by Murchison 6 were associated with carcinoma of the gall-bladder. Faeces may pass through a cholecystocolic fistula into the gall-bladder and set up suppuration in the liver.

This is exemplified in the following case in St. George's Hospital. A woman aged thirty-one years had had jaundice, without any definite biliary colic, for one and a half years before her death; the jaundice varied from time to time but became very dark before death. She was thought to have malignant disease, and an exploratory operation was performed, but it was impossible to do anything. At the necropsy the gall-bladder had ulcerated into the colon, and the parts around were firmly matted together by dense adhesions. There were gall-stones and faeces in the gall-bladder, the right hepatic duct contained faecal material, and there were multiple abscesses in the liver (*vide* Plate VII).

Fistulae between the Biliary Tract and the Small Intestine.—A direct communication between the gall-bladder or ducts and any part of the small intestine except the duodenum is most exceptional, and hardly any cases are on record. The small intestine is, from its position and free mobility, less likely to become adherent to the gall-bladder. Naunyn¹ refers to 1 case in which the jejunum (Gaston), and another in which the ileum, communicated with the gall-bladder.

Results of the Passage of Calculi into the Intestines.—In addition to causing mechanical obstruction of the bowel, which is described on p. 751, a calculus may damage the wall of the intestine and lead to the formation of a diverticulum containing the calculus, or even to gangrene. In exceptional instances a small gall-stone has passed into the vermiform appendix, and been found on removal of the inflamed appendix; the presence of calculi would favour infection and inflammation. Undoubted examples have been recorded by Kelly and Hurdon² (2), Mayo Robson,³ Lediard,⁴ Wynne and Sturm.⁵ Gall-stones have also been found in a Meckel's diverticulum (Sherren⁶). As the result of ulceration between the gall-bladder and duodenum or colon cicatricial contraction and stricture of the bowel may occur. Cicatrization of a fistula is, however, rare (Naunyn) or is rarely recognised at the necropsy.

¹ Naunyn. *On Cholelithiasis*, p. 148.

² Kelly and Hurdon. *The Vermiform Appendix and its Diseases*, p. 363, 1905.

³ Mayo Robson. *Lancet*, Lond., 1906, ii, 1768.

⁴ Lediard. *Ibid.*, 1907, i, 83.

⁵ Wynne and Sturm. *Brit. Med. Journ.*, 1909, ii, 515.

⁶ Sherren. *Proc. Roy. Soc. Med.*, 1910, iii (Clin. Sect.), 11.

It may be suspected, when, as in Goldschmidt's case,
a large Calculus is passed per anum. without any
~~marked~~ intestinal symptoms

Goldschmidt. Bull. et mém. Soc. méd. des hôp. de Paris, 1913, 3. s., xxix, 973.

PLATE VII.



SECTION OF LIVER SHIEWING ABSCESSES DUE TO INFECTION OF THE BILE-DUCTS IN A CASE OF
CHOLECYSTOCOLIC FISTULA FROM CHOLELITHIASIS.

(Dronby, H. H. G.
J. C. G. A. V. 1890)

Burgess/1

Right sided or diaphragmatic
pleurisy may precede the
formation of the fistula. / 1

Burgess. Brit. Journ. Surg. / 1
1921, ix, 253

Broncho-biliary Fistulae.—In ~~40~~⁴⁶ cases of this condition collected by Ido and Yasuda,¹ 26, or ~~32~~ per cent, were due to cholelithiasis. As cholelithiasis is the most frequent cause of broncho-biliary fistulae, a general account of the condition will be given here. Gall-stones may give rise to a broncho-biliary fistula in several ways: (a) Gall-stones in the common duct set up infective cholangitis and an abscess in the liver which perforates the diaphragm and, after setting up adhesions between the diaphragm and the base of the lung, ruptures into the latter; or the liver abscess may perforate first into the pleura and subsequently into the lung. (b) Intrahepatic calculi may give rise to a similar sequence of events. (c) A calculus may ulcerate out of the gall-bladder or ducts, and set up an intra-peritoneal abscess which perforates the diaphragm and either opens into the lung direct or first into the pleura and subsequently into the lung. (d) A suppurating gall-bladder associated with cholelithiasis may set up a subphrenic abscess which perforates the diaphragm and eventually opens into the lung. (e) In very rare cases, as in Mandard's,² the gall-bladder may perforate directly through the diaphragm into the lung.

Symptoms.—Irritating cough may be accompanied by orthopnoea and the expectoration of large quantities of bile, sometimes almost pure; Graham³ speaks of expectoration of as much as 700 c.cm. of bile in the twenty-four hours. A few patients have coughed up biliary calculi.

Signs.—There may be dullness in the right inframammary and axillary regions, extending back for a variable extent, the breath-sounds over this area being coarse and accompanied by rales. On the other hand, there may be no dullness on percussion, and merely bronchitis. When the discharge of bile is free, there may be no jaundice and no bile in the urine, ~~as in Smith and Rigby's~~⁴ ~~case~~.

The cough is likely to be worse in the recumbent position.

The diagnosis depends on the copious expectoration of bile. In jaundiced patients with bronchitis or pneumonia the sputum is bile-stained, but the amount of bile is much less. Fragments of liver tissue may also be found in the sputum. The cause of a broncho-biliary fistula may be obscure; other signs of cholelithiasis, or in rare cases the expectoration of biliary calculi, hydatid membrane, or round worms, would settle the diagnosis.

Prognosis.—Recovery may occur spontaneously or after operative interference on the biliary apparatus. When spontaneous recovery occurs, there is, generally speaking, no liability to return of the fistula; a relapse has, however, been known to occur.

A patient, after expectorating bile, was free for ten years from any symptoms; they then recurred and proved fatal (J. E. Graham).

Treatment.—If the condition does not tend to pass away and undergo spontaneous cure, laparotomy, with the view of removing the obstruction

¹ Ido and Yasuda. *Repts. n. path. Anat. n. n. allg. Path.*, Jena, 1912, iii, 567.

² Mandard. *Thèse de Paris*, 1854. Quoted by Naunyn.

³ Graham, J. E. *Trans. Assoc. Am. Phys.*, Phila., 1897, xii, 247.

⁴ Smith and Rigby. *Brit. Med. Journ.*, 1903, ii, 313. *Repert. Practitioner*, Lond., 1912, Lxxxix, 718.

to the passage of bile into the intestine, should be undertaken; when the gall-stones are removed from the common duet, the fistulous channel into the lung should heal up.

Other and rare forms of Fistulae.—Fistulae between the bile-ducts themselves.—Naunyn,¹ who quotes 8 cases, adds that they are merely of anatomical interest.

Fistulae between the gall-bladder and the portal vein are very rare; Naunyn quotes 3 cases, but does not admit Bristowe's² case. According to tradition there were three calculi in the portal vein of Ignatius Loyola, but Thudichum³ emphatically states they were phleboliths; possibly the calculi were really in the common bile-duet, which was mistaken for the portal vein. Ulceration of a calculus into the portal vein would, of course, tend to set up suppurative pylephlebitis.

Ulceration of the Hepatic Artery.—A communication between the gall-bladder or the bile-ducts and the hepatic artery or its branches leads to profuse or even fatal haemorrhage which runs down the ducts into the alimentary canal. These cases may be regarded as examples of aneurysms of the hepatic artery or its branches, rupturing into the biliary tract. But it must be remembered that ulceration of the gall-bladder or bile-ducts in cholelithiasis may erode the walls of the hepatic artery or its branches and first give rise to an aneurysmal bulging and subsequently to rupture of the vessel into the biliary tract (*vide* also p. 45).

According to Naunyn,⁴ Lebert's case of hepatic aneurysm rupturing into the gall-bladder was probably of this nature; M. B. Schmidt recorded a case of ulceration of a bile-duct, due to a calculus, producing hepatic aneurysm.

Fistulae between the gall-bladder and the kidneys are also very rare. Courvoisier⁵ quoted 5 cases. The fistulous passage is usually between the gall-bladder and the pelvis of the right kidney. An abscess formed after perforation of the gall-bladder may open into the pelvis of the right kidney and enable biliary calculi to escape from the body by the urinary tract (Jones⁶). Elsner⁷ reported another case with a gall-stone in the pelvis of the right kidney.

Fistulae between the Gall-bladder and Urinary Bladder, etc.—Barnard⁸ refers to a number of cases. H. Faber, in 1839, wrote an octavo volume on the subject. Köstlin and Wucherer have described fistulae, and Abt, Güterbock,⁹ Hahn, ~~and~~ Michel¹⁰ biliary calculi in the urinary bladder. In fistulae between the urinary and biliary tracts bile may appear in the urine without jaundice.

¹ Naunyn. *On Cholelithiasis*, p. 149. Transl. New Sydenham Soc., 1896.

² Bristowe. *Trans. Path. Soc.*, Lond., 1858, ix, 285.

³ Thudichum. *A Treatise on Gall-stones*, p. 11, 1863.

⁴ Naunyn. *Loc. cit.*, p. 141.

⁵ Courvoisier. *Pathologie u. Chirurgie der Gallenwege*, 1890.

⁶ Jones, T. C. L. *Lancet*, Lond., 1907, i, 1085.

⁷ Elsner. *Med. News*, N.Y., 1898, lxxii, 164.

⁸ Barnard, H. L. *Ann. Surg.*, 1902, xxxvi, 161.

⁹ Güterbock. *Virchows Arch.*, 1876, lxvi, 273.

¹⁰ Michel. *Zentralbl. f. Gynäk.*, Leipz., 1909, xxxiii, 25.

^ | MacDonald

Kronlein and Bergmann recorded cases in which calculi reached the urinary bladder from a patent urachus in communication with the gall bladder.

MacDonald, S. Proc. Roy. Soc. Med., 1924, xvii, (Sect. Urol.) 23.



A case of cholecysto-vaginal fistula has been reported. It is quite conceivable that an elongated gall-bladder with an abscess in connexion with it may track into the pelvis.

A communication between the *pericardium* and the *biliary tract* is one of the rarest fistulae. In 1892 Naunyn only knew of 1 case. An abscess on the surface of the left lobe of the liver, secondary to intrahepatic cholangitis set up by a calculus in the common bile-duct, opened in a case of Legg's¹ into the pericardium.

Rupture and Perforation of the Gall-bladder into the Peritoneum.—It is most unlikely that a healthy gall-bladder would rupture merely from the weight of contained gall-stones, but, as a matter of fact, the gall-bladder is seldom healthy in cholelithiasis. It may be thinned from distension, and rupture may then take place from trauma, or as the result of sudden pressure brought to bear on the gall-bladder by contraction of the abdominal walls in violent straining, coughing, etc., or in the vigorous abdominal contractions of delivery. In such cases there may be no active inflammation or previous ulceration of the gall-bladder. If the bile is sterile, the peritoneum may suffer little. Cases have occurred in which large quantities of bile have been removed from the abdominal cavity, but this chiefly occurs when a hydatid cyst in communication with a bile-duct ruptures into the peritoneum (*vide* p. 416). Usually rupture of the gall-bladder is disposed to by recent inflammation of its walls or by definite ulceration, and the infective contents of the gall-bladder readily set up generalised peritonitis.

In some instances, as the result of adhesions around the gall-bladder, the rupture or perforation sets up a localised peritoneal abscess, which may contain calculi, in communication with the gall-bladder. An abscess of this kind may open either on the surface of the body or into one, or even into several, of the abdominal or thoracic viscera, and thus give rise to fistulae, which may be multiple and extremely complicated. In rare instances a localised abscess forms behind the peritoneum, the gall-bladder having become adherent to the posterior abdominal wall. In other cases calculi may ulcerate out of the gall-bladder and be found surrounded by adhesions.

Moynihan² described a case in which three gall-stones, each the size of a Barcelona nut, had ulcerated almost through the walls of a gall-bladder with chronic sclerosing cholecystitis. Two of these calculi lay in pockets in the omentum and the third was almost hidden in a cavity in the liver. In a lunatic numerous calculi were found firmly adherent to the peritoneum in various parts of the abdomen (Gillespie³).

Treatment.—*Prophylaxis.*—In fat people, especially women, and after enteric fever, influenza, malaria, and pregnancy, it may sometimes be within the medical man's power to advise a change in the patient's mode of life which will tend to prevent, or diminish the liability to, catarrhal

¹ Legg, J. W. *Trans. Path. Soc.*, Lond., 1874, xxv, 133.

² Moynihan. *Brit. Med. Journ.*, 1903, i, 186.

³ Gillespie. *Ibid.*, 1905, i, 990.

inflammation of the gall-bladder and bile-ducts and stagnation of bile. These measures are, in the main, on the same lines as those for the general hygienic treatment of cholelithiasis in the intervals between the attacks. Thus gentle exercise, in the fresh air if possible, short of fatigue, so as to favour the passage of bile into the intestine, is advisable. When this is not practicable, breathing exercises to increase the movements of the diaphragm and liver should be instituted. Stooping over desks and working in a cramped position must be corrected, and the use of tight corsets and belts should be discontinued. The patient should be warmly clad, so as to avoid chills. In enteric fever the bile constantly contains the pathogenetic organism, and it is therefore reasonable during the course of the fever and in convalescence to give short courses of urotropin. A visit to one of the spas mentioned on page 779 is a valuable precautionary measure.

THE GENERAL MEDICAL TREATMENT of cholelithiasis and its various manifestations may be considered under the following heads: (1) To prevent stagnation of bile. (2) To prevent the occurrence of catarrhal inflammation of the gall-bladder and bile-ducts. (3) To remove catarrhal inflammation when it has appeared. (4) Attempts to dissolve calculi. (5) Attempts to remove calculi. (6) Spa treatment. (7) Diet.

(1) **To Prevent Stagnation of Bile.**—Exercise leads to increased movements of the diaphragm and liver and so to an increased flow of bile into the duodenum. In comparatively young and vigorous persons active exercise, rather than a "constitutional" walk, is needed. Horse exercise is perhaps the best, but bicycling, climbing, tennis, and rowing are excellent. In cases in which active open-air exercise is not possible, deep respirations should be practised so as to induce vigorous movements of the diaphragm and liver, and in some cases abdominal massage is useful in increasing the tone of the abdominal muscles and the flow of bile. After pregnancy the lax condition of the abdominal wall, which favours enteroptosis, hepatoptosis, and stagnation of bile, may be met by massage to the abdominal muscles, care being taken not to bring direct pressure to bear on the gall-bladder, since cholecystitis may thus be set up.

The factor of dress, especially the corset, tight waist-bands, and heavy skirts, in constricting the lower part of the chest and preventing free diaphragmatic respiration, has been referred to in the consideration of the greater incidence of gall-stones in women (*vide* p. 723). These causes should be obviated, and the wearing of tight belts in men discontinued.

By the Administration of Food and Drink.—When food passes into the duodenum, bile is driven out of the gall-bladder into the duodenum. Meals at short intervals, therefore, are effective in preventing biliary stagnation. In addition to meals at comparatively short intervals some supper should be eaten before going to bed, and it is a good plan to have light food available, so that in case the individual wakes, a small meal

may be taken during the night. The subject of the diet will be referred to later (*vide* p. 779).

Though experimental results shew that water cannot be considered a cholagogue, good results undoubtedly follow the taking of large draughts of hot water. Carlsbad, Harrogate old sulphur, Vichy, and Contrexéville waters have a good effect, or hot water containing some sulphate or phosphate of sodium. The action of an increased amount of water is probably complex: the bile is diluted and rendered more copious, while catarrh of the ducts and intestine is relieved. In order to get the maximum effect from water it should be taken before meals, when the stomach is empty. Thus it may be taken the last thing at night or, as is more frequently done, early in the morning. It should then be sipped in the intervals of dressing, or later in the day while walking about in a garden.

The water should, of course, not be taken in excessive quantities or too hot, otherwise dilatation of the stomach may occur. Dr. Whittick has told me of a patient who, having a little knowledge of medicine, treated himself for gall-stones by copious draughts of water as hot as he could bear, and as a result developed very acute dilatation of the stomach which nearly proved fatal.

Copious enemas of hot water have been recommended and have been thought to induce muscular contraction of the gall-bladder and expulsion of the contained bile.

Cholagogues.—Although a number of drugs have been credited with the power of increasing the secretion and flow of bile, it is probable that salicylate of sodium and bile itself are the only drugs which really increase the secretion of bile. Mercurey, podophyllin, iridin, rhubarb, senna, aloes, turpentine, and other drugs may excite peristaltic contraction of the ducts and so lead to a temporary increase in the amount of bile discharged into the duodenum, but do not really augment the secretion of bile (Rutherford and Vignal,¹ Mayo Robson²). Toluylenediamine at first increases the flow of bile, but later the bile becomes more viscid from a larger quantity of mucus in it. This body has only very occasionally been employed in medicine, and is dangerous from its haemolytic or destructive action on the red blood-corpuscles and its tendency to produce inflammation of the small bile-ducts and jaundice (*vide* p. 533).

Secretin, which, as Starling and Bayliss³ have shewn, is manufactured in the duodenal mucous membrane and stimulates the secretion of the pancreas, also increases the secretion of bile.

Ox or pig's bile is sometimes given in capsules, but it is better to give the salts of the bile acids alone, since the bile-pigments are themselves somewhat poisonous.

¹ Rutherford and Vignal. *Journ. Anat. and Physiol.*, 1876, x, 253.

² Mayo Robson. *Proc. Roy. Soc.*, Lond., 1890, xlvii, 21.

³ Starling and Bayliss. *Ibid.*, 1902, lxix, 352.

Gautier¹ met with complete relief from attacks of biliary colic, which had extended over five years, after a prolonged course of ox bile.

Salicylate of sodium has the advantage that it not only increases the secretion of bile, but that it acts as an intestinal antiseptic and so tends to diminish intestinal catarrh. It may be given in 10-grain doses twice or three times daily with an equal quantity of bicarbonate of sodium. The most satisfactory treatment from the point of view of inducing an increased flow of bile is to give salicylate of sodium combined with plenty of alkaline waters. Aspirin (salicylacetic acid) may also be given, but is incompatible with bicarbonate of sodium. Salicylate of sodium may advantageously be combined with urotropin, which is excreted into the biliary tract (Crowe²) and ~~may~~ exert an antiseptic influence; calcium chloride ~~may be added to counteract haemorrhage or itching.~~

(Knott) ^
 Chauffard³ combines salicylate of sodium (gr. x) with benzoate of sodium (gr. iii) three times daily for periods of twenty, fifteen, or ten days in every month for a year or two, the duration of the course diminishing as time goes on. Iodide of potassium has been stated to check frequent attacks of colic. Its method of action is doubtful; possibly it may increase the mucous secretion from the walls of the biliary tract and so augment the flow of fluid through the ducts and thus relieve catarrh. It is also conceivable that, like chloroform and ether, it may diminish spasm.

(2) To Prevent Catarrhal Inflammation.—Indigestion and gastritis, which, by leading to gastro-duodenal catarrh, might set up catarrhal inflammation of the bile-ducts, must be treated by careful dieting, drugs, and the prevention of constipation. The food should be bland, nutritious, and eaten slowly. The condition of the teeth should be seen to, so that the food can be properly masticated, and further that there is no oral sepsis to set up gastritis. Worry and anxiety frequently cause dyspepsia, and in this way favour infection of the ducts and gall-bladder. Constipation and the attendant liability to indigestion and gastro-intestinal fermentation and putrefaction should be prevented by gentle purgatives; vigorous purges must be avoided, as enteritis may thus be induced. Salines such as half a tumbler of natural Carlsbad water with a little hot water before breakfast, or one or two drams of Carlsbad salts dissolved in hot water are useful. Phosphate of sodium in dram doses may also be given in water early in the morning. The Carlsbad salts are better borne by the stomach if a little infusion of quassia or cinchona is added to the draught. While sipping the salts the patient should walk about, or better, practise systematic exercises with deep inspiratory movements so as to favour the descent of the diaphragm, and should not have any food until an hour after the draught has been taken.

¹ Gautier. *Rev. méd. de la Suisse Rom.*, Genève, 1898, xviii, 318.

² Crowe. *Johns Hopkins Hosp. Bull.*, Balt., 1908, xix, 109.

³ Chauffard. *Traité de méd.* (Bouchard, Brissaud), 1902, v, 85.

lactate, ^{for etching} or hypodermic injections of horse serum, which Gibbon considers practically eliminates the risks of operative haemorrhage, may also be given. Whipple ~~marks~~ prefers intravenous injection of 0.2 per cent. calcium lactate solution up to 500 c.c.

Knott, F.A. Guy's Hosp. Rep., 1923, LXXIII, 195

Gibbon, J.H. Trans. Coll. Phys., Phila., 1917, 3 ser., XXXIX, 243

Whipple, A.O. Ann. Surg., 1918, LXVIII, 471.

Hansemann

j Crowe found that 75 grains
 daily were necessary in order
 to render the bile sterile.
 It may be given per rectum, or
 2 or 3 grains may be added to every
 ounce of water, or in this way
 100 grains may be taken daily.
 The tendency to irritate the urinary
 bladder is said to depend on the
 liberation of formalin in acid
 urine, and hence if the urine is
 kept alkaline these symptoms should
 not occur. Hurst gives a single
 dose at night of potassium
 citrate 3i, sodium salicylate grss,
 hexamine grss increased by grss
 each night ~~and~~ ^{up to} 10 grains x.c. or
 until vesical irritation appears.

V. Hansemann. Virchows Arch. 1910, CXXII, 139.

^{S.J.} Crowe, Johns Hopkins Hosp. Bull., Balt., 1912, XXIII, 255.

HURST, A.F. Practitioner, London 1923, Cxi, 321

(3) **To Remove Catarrhal Inflammation of the Biliary and Intestinal Tracts.**—It is important to remove inflammation of the gall-bladder, because calculi are formed as a result of catarrhal cholecystitis and are not likely to be dissolved so long as the gall-bladder is inflamed. Harley and Barratt¹, and Bain,² experimenting with dogs, have shewn that calculi are dissolved by the bile in healthy gall-bladders, but not in the presence of cholecystitis. As the gall-bladder of patients with calculi is usually affected, there is little chance that calculi will be dissolved.

The methods already referred to, by which the flow of bile is increased and the bile-passages washed down, are of use in removing catarrhal inflammation of the gall-bladder and bile-ducts. Urotropin is of great use for its disinfecting action. Carlsbad salts, phosphate of sodium, Epsom salts in hot water, or table waters, such as Contrexéville and Homburg, should be taken so as to remove catarrhal inflammation of the intestines and to keep the bowels loose. Vigorous purgatives should be avoided, as they tend to set up inflammation of the mucous membrane.

The abdomen should be kept warm; and when there is tenderness over the gall-bladder poultices, hot packs, or fomentations, or heat by means of the thermophore, may be applied over the right hypochondrium.

A. E. Wright³ suggested that patients should be immunised against the colon bacillus, so as to arrest cholecystitis due to infection with *B. coli*, so that the calculi might gradually dissolve in the bile. Cholecystitis with a persistent fistula after operations for gall-stones has been benefited by vaccines of *B. coli* (Wright and Reid⁴).

(4) **Attempts to Dissolve Calculi.**—Numerous drugs have been tried and recommended with a view to dissolving calculi, but with very little, if any, success. Naunyn estimated that this is effected in about 1 per cent of the cases. A very famous, ancient remedy was Durande's, which consisted of a mixture of ether (℥ xv) and turpentine (℥ x) in a capsule. Although this remedy may do good by virtue of the antispasmodic action of ether or of the expulsive action of turpentine—radically opposed as these actions are—there is no reason to believe that the calculi in the gall-bladder are acted upon directly by the drugs. Chloroform, which has been employed as a solvent, probably acts chiefly as an antispasmodic.

Olive oil has been widely used to relieve the symptoms of cholelithiasis. It has been proved to dissolve calculi in a test-tube (Brockbank,⁵ L. Scott⁶), but there is no evidence that olive oil given by the mouth, much less when injected per rectum, can act on calculi in the gall-bladder. In fact, there is a well-known fallacy about some of the good effects ascribed to its use, namely, that the oil itself may be so

¹ Harley and Barratt. *Journ. Physiol.*, 1903, xxix, 341.

² Bain. *Brit. Med. Journ.*, 1905, ii, 269.

³ Wright, A. E. *Ibid.*, 1903, i, 1073.

⁴ Wright and Reid. *Ibid.*, 1906, i, 143.

⁵ Brockbank. *Med. Chron.*, Manchester, 1893-4, xix, 155.

⁶ Lindley Scott. *Brit. Med. Journ.*, 1897, ii, 798.

HEXAMETHYLENAMINE

digested and altered as to imitate softened calculi when passed by the bowel.

Delépine¹ described the case of a patient who took olive oil for cholelithiasis and passed 40 round or oval bodies which were at first regarded as biliary calculi and as evidence of the success of the treatment. They turned out to be masses of crystals of fatty acids derived from the oil.

It is conceivable, however, that olive oil might exert a solvent action on a calculus impacted in the actual orifice of the biliary papilla. It has also been thought that fatty acids and glycerin absorbed from the bowel may reach the liver and lead to an increased flow of bile into the gall-bladder. Bile acids dissolve cholesterin, hence the more bile passes over a calculus, the better the chance of some absorption taking place. Some of the good effects of oil may be due to its power of inhibiting hyperchlorhydria and to its soothing and antispasmodic action on the intestine. Olive oil is given in quantities of from 6 to 12 ounces a day by the mouth, but is far from a pleasant thing to take. Some writers, however, speak highly of the good effects of olive oil in cholelithiasis. Pure olive acid (Merck) and eunatrol, or pure oleate of sodium, and glycerin, have been recommended instead of the oil. ~~Fat and cream may also be taken in place of the oil, unless they disturb digestion.~~

Since the bile acids dissolve cholesterin, any increase in the secretion of bile, such as is induced by salicylates or by the administration of bile by the mouth, may be regarded as a means of dissolving calculi. Since protein food increases the percentage of bile acids in the bile, meat has been regarded as an important element in the diet of patients suffering from gall-stones; but, as it has recently been shewn that a protein diet also increases the amount of cholesterin in the bile, this argument is not of much weight. As already pointed out, V. Harley and Barratt's² experiments shew that calculi are dissolved by the bile provided cholecystitis is absent. It is, therefore, important to prevent or remove inflammation of the gall-bladder, and for this purpose urotropin and salicylate of sodium, ~~or their combination in the form of saliformin,~~ are advisable. Partly on experimental grounds and partly on clinical observation, Bain² recommends Harrogate old sulphur water and urotropin combined with iridin as solvents of gall-stones.

(5) **Attempts to Remove Gall-stones.**—Measures, such as massage, and drugs, such as turpentine and purgatives, which lead to muscular contraction of the gall-bladder and bile-ducts, have been employed to favour the expulsion of calculi. At the commencement of a course at Carlsbad it not uncommonly happens that a patient experiences an attack of biliary colic and passes calculi. Increasing the flow of bile by salicylates and ox-bile cannot be regarded as likely to drive calculi out of the gall-bladder, though their good effects in reducing catarrh of the ducts and the possibility that calculi may, as already pointed out, be dissolved,

¹ Delépine, S. *Trans. Path. Soc.*, Lond., 1890, xli, 111.

² Bain. *Brit. Med. Journ.*, 1905, ii, 269.

and Hansemann's

^{they used}
but the dogs in which the cholesterol content of
the bile is lower ~~than~~ than in man, and further
their gall bladders were normal; so it is
doubtful if these results can be applied to man.

Hansemann

Virchow's Arch., 1913, CCxii, 139

A high cholesterol^{ol} content of the blood favours the formation of cholesterol^{ol} calculi. The cholesterol^{ol} comes ~~almost entirely~~ from the food, but some persons have a tendency to retain cholesterol^{ol} and develop hypocholesterol^{ol} aemia, just as others tend to retain uric acid. A diet poor in fats and ~~so valued to form~~ ^{broths, eggs} cholesterol is advisable, and ^{stewes, fried food, game, duck, kidneys, etc.} Cream, butter, ^{eggs, meat, and} Liver, and sweetened ~~fat~~ should be avoided. Vegetables, with the exception of beans and peas which are fairly rich in phyla-cholesterol^{ol}, and skimmed milk should be taken.

Rothschild and Rosenthal advise a lipid-free diet on 3 or 4 days out of the week.

~~must not be forgotten.~~ Measures intended to lead to the expulsion of gall-stones are uncertain in their action. Massage of the gall-bladder and bile-ducts in order to effect "the extrusion of gall-stones by digital manipulation" was advocated by George Harley¹ in 1888, and ~~has been~~ ^{has} ~~condemned as~~ a dangerous method of working in the dark. No doubt it might lead to the expulsion of soft calculous masses lying in the common bile-duct, but in many cases it would be quite powerless to do any good and might easily do harm by leading to rupture of an ulcerated gall-bladder or duct. If it were possible to recognise with certainty cases with soft calculous material in the common duct, gentle massage might be recommended, but, unfortunately, our methods of diagnosis are not sufficiently sure to enable us to do so.

(6) **Spa Treatment.**—Mineral waters dilute and increase the flow of bile and may thus lead to some degree of solution of calculi in the ducts and gall-bladder and to their ultimate discharge into the duodenum. The increased flow of bile flushes the bile-ducts and thus tends to remove infective catarrh, and so to prevent the further formation of calculi and possibly to favour absorption of calculi. It is not absolutely necessary to go to a spa in order to undergo the treatment, for it can be carried out under medical advice at home; but the patient probably gains by going to the original source, from the change of scene and from the influence exerted by the regular life, the régime, and the freedom from business cares and worries. Hot Carlsbad water should be sipped while walking up and down an hour before breakfast and in the afternoon, about $\frac{3}{4}$ pint being taken on each occasion and three-quarters of an hour being devoted to the process. The taste of the salts is less disagreeable if some infusion of quassia or cinchona is added. No food should be taken until an hour after the last dose of water is taken.

Carlsbad, Vichy, Marienbad, Kissingen, Homburg, Neuenahr, Ems, Bertrich, Brides, are appropriate spas on the Continent. In England Harrogate, Llandrindod Wells, enjoy some reputation, while in America Bedford, Pa., Las Vegas Hot Springs, Sharon, White Sulphur, are recommended for the treatment of gall-stones. At Carlsbad and Vichy calculi are not infrequently passed after the treatment has begun; patients should, therefore, be warned that they may have a return of colic with jaundice. Neuenahr and Bertrich are less depressing than Carlsbad; the waters at Salzschlirf, Wiesbaden, Nauheim, and Soden are sometimes recommended.

(7) **Diet.**—Food should be taken at comparatively short intervals and the amount at each meal should not be large; overeating must, of course, be prevented. As to the kind of food most suitable for patients with gall-stones, considerable divergence of opinion has been expressed. It is unnecessary to insist that the food should be digestible and not too bulky. The amount of starchy food should be much restricted, and bread should be taken sparingly and preferably as toast, sugar in small quantities only, and porridge and rice in moderation. It is particularly

¹ Harley, G. *Illust. Med. News*, Lond., 1888-9, i, 73.

with regard to fatty food that contradictory statements have been made. Some writers believe that fat favours the production of calculi; others that fats are indicated as solvents of gall-stones. It is probable that fatty food has no particular action in dissolving calculi in the bile-ducts or gall-bladder, and that it only does harm indirectly, viz. when it gives rise to acid dyspepsia. As a general rule, fatty food should be taken in small quantities and carefully watched; when any signs of dyspepsia or fermentation appear, it should be diminished in amount, or, if need be, discontinued. Protein food may be taken with greater freedom in the form of mutton, beef, game in small quantities, and vegetables containing a good deal of albumin. Alcohol is best avoided, and if required for other reasons, should be well diluted. Light claret, still Moselle, or a little whisky may be taken in this way. Beer, stout, champagne, and especially liqueurs should be forbidden. The importance of taking plenty of water before meals has already been insisted on.

SURGICAL TREATMENT.—It has already been pointed out that in acute biliary colic operative interference is justifiable only when life is threatened by some extremely grave complication, such as rupture of the gall-bladder or bile-ducts with resulting peritonitis, or when, as rarely happens, concomitant acute infective cholecystitis sets up widespread peritonitis, or when signs of acute intestinal obstruction appear. There is naturally considerable difference of opinion as to the indications for operative interference in gall-stones. Moynihan¹ is of opinion that as soon as gall-stones are known to be present in the gall-bladder the safest, the speediest, and the only proper course is to remove them, and that the only contraindication is the presence of some morbid condition which would render operation dangerous.

The effects of cholelithiasis which require surgical interference may be arranged as follows:

(i) When there is acute inflammation in the region of the gall-bladder with the signs of severe localised peritonitis.

(ii) When, in a case with a history of gall-stones, there are symptoms pointing to acute perforative peritonitis, such as might be set up by perforation of the gall-bladder.

(iii) When, from the presence of fever, pain, jaundice, etc., there is evidence that severe infective inflammation of the bile-ducts has developed. Under these conditions the gall-bladder and ducts should be freely drained.

(iv) When acute intestinal obstruction occurs in patients with a history of gall-stones.

(v) When there is a large tumour constantly present in the position of the gall-bladder, such as might be due to distension of the gall-bladder by serous or mucous fluid (dropsy of the gall-bladder), by pus (empyema), or by a collection of calculi.

(vi) When jaundice in a patient with a history of gall-stones becomes chronic. The period which should be allowed to elapse after the onset

¹ Moynihan. *Practitioner*, Lond., 1908, lxxxii, 835.

of permanent jaundice varies very considerably. Hanot fixed the period at three months; Boix¹ shortened it to six weeks; and C. Beck² argued in favour of four weeks. If medical measures are quite ineffectual and the patient loses ground, the chance of relief from operation is certainly diminished by delay, as the liver cells are further damaged by the prolonged stagnation of the bile in the intrahepatic bile-ducts. There is also the danger that suppuration may supervene in the dilated bile-ducts or in the liver. Further, the marked tendency to haemorrhage which exists in so many deeply jaundiced patients makes operative interference difficult and dangerous. No rigid rule can be laid down as to the time which should be allowed to elapse before a patient with chronic jaundice is operated upon. The patient's condition, general nutrition, presence or absence of symptoms, and response to treatment must all be considered. If improvement occurs under medical treatment, it would obviously be unwise to adopt operative measures. As a general rule, operation should be advised earlier in poor patients whose livelihood depends on their ability to work than in well-to-do patients who can afford a cure at Carlsbad, Neuenahr, and other spas.

(vii) In intermittent hepatic fever, in which there is a calculus in the common bile-duct which sets up recurrent attacks of fever, pain, and jaundice, medical treatment should always be given a good trial, and if the attacks become less frequent and severe and gradually disappear, there is, of course, no need for operation. On the other hand, if the attacks become more frequent or no improvement occurs, operation should be considered and should be carried out before the patient becomes too run down in strength and resistance.

(vii) In recurrent biliary colic, without the passage of calculi in the stools, which leads to serious impairment of the patient's health and threatens to induce a condition of chronic invalidism, the question of operative interference must be considered. A poor man who cannot afford the loss of time and expense involved by a cure at Carlsbad, Neuenahr, Harrogate, etc., should be advised to submit to operation. A rich patient should be given the chance of a course of spa treatment under careful medical supervision before an operation is undertaken. An additional reason for operating in some cases is that carcinoma of the gall-bladder occurs in from 14 to 4 per cent of all the persons with gall-stones, and that removal of the gall-stones and, if necessary, of the gall-bladder may prevent this sequel. In a case of recurrent attacks of biliary colic it would probably be safer to advise operative interference at any earlier date in patients who have a family history of carcinoma than in other patients. The patient's condition, strength, and power of resistance must be considered in deciding on operative interference.

(ix) When, from adhesions between the gall-bladder and pyloric end of the stomach, continued and severe gastric symptoms are produced (*vide* p. 758).

¹ Boix. *Arch. gén. de méd.*, Paris, 1901, clxxxviii, 470.

² Carl Beck. *Méd. Week*, Paris, 1897, v. 137.

(x) In patients who are acquiring the morphine habit as the result of prolonged suffering operative interference is necessary to prevent the establishment of this pernicious habit.

(xi) In some cases of fistulae, both external and internal.

For the details of the operations the reader must consult the text-books on operative surgery. The question of recurrence after operation is dealt with on p. 743.

The question of cholecystectomy or cholecystotomy requires careful consideration in every case; but when the gall bladder is chronically inflamed removal is now recognized as the most certain method of securing a cure.

It has been urged that the more complete operation is likely to be attended by a higher mortality.

When the cases are carefully selected, cholecystectomy may give a lower mortality; at the Mayo Clinic ~~between~~ 1907 and 1916 there were 2493 cholecystectomies with a percentage of 1.3, and 2854 cholecystotomies with 1.5 per cent. mortality (C.H. MAYO).

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